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THE TREATMENT OF RHEUMATOID ARTHRITIS WITH 417 COURSES OF GOLD*

An Analysis of 259 Cases

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MUCH has been written on the subject of gold as a therapeutic agent in the treatment of rheumatoid arthritis. Its merits are apparently undeniable, but its mode of action is still a matter of conjecture. There seems to be general agreement that gold is a dangerous drug and that extreme caution must be exercised in its administration. In this paper we wish to emphasize the matter of untoward reactions and the lack of influence of vitamin therapy on reactions as well as on treatment.

In 1943, two of us[1] reported the results of the treatment of 122 cases of rheumatoid arthritis receiving 176 courses of gold. In that report only 11 per cent untoward reactions were observed, this figure being based on the total number of courses given. Compared with the reports of other workers, this percentage was considered unusually low. The patients received, in conjunction with gold therapy, large amounts of orange juice and liver, and it was thought that one of these factors might have been responsible for the low incidence of untoward reactions.

On the basis of the above, treatment was begun with three new groups of cases. Gold was administered as in the previous study. Solganal-B Oleosum¶ was given intramuscularly in the following dosage: 10 mg. twice weekly, 4 doses; 25 mg. twice weekly, 4 doses; 50 mg. twice weekly, 4 doses; and 100 mg. weekly, 9 doses. This constituted a course. A rest period of at least six weeks was allowed between courses. One group received orally with the above 300 mg. of ascorbic acid daily, and another group received 2 teaspoonfuls of vitamin B complex three times daily.|| Since most of the cases were ambulatory, it was deemed advisable to use Vitamin B complex orally in place of liver. This substance was more desirable since it permitted the elimination of another injectable preparation. A third group received gold without vitamins. Table 1 shows the number of cases treated by this method and the number of courses of gold received. We attempted by this method to determine whether one of the above factors might be considered a necessary adjunct to the treatment of rheumatoid arthritis, as well as an aid in the reduction of untoward reactions.

TABLE 1. *Cases Listed according to Number of Courses and Type of Treatment.*

TYPE OF TREATMENT	NUMBER OF COURSES					TOTAL
	1	2	3	4	5	
Gold and vitamin C	65	35	11	6	1	118
Gold and vitamin B complex	29	16	11	8	2	66
Gold alone	43	7	3	2	2	57
Totals	137	58	25	16	5	241

As in the previous study,[1] patients were classified according to the grade of the disease and the improvement, as follows:

Class 1. Typical rheumatoid arthritis of less than one year's duration (subjective symptoms only).
Class 2. Changes in joints, with activity only slightly limited.
Class 3. Changes in joints, with greatly limited activity.
Class 4. Dislocations, ankyloses and contractures (patient confined to bed or wheel chair).

Group 1. No improvement (NI).
Group 2. Improved (I).
Group 3. Much improved (MI).
Group 4. Very much improved (VMI).

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¶Gold in the form of Solganal-B Oleosum was kindly supplied by Schering Corporation, Bloomfield, New Jersey, through the courtesy of Dr. Max Gilbert.

||The ascorbic acid and the vitamin B complex (Elixir Plebex) were kindly supplied by Wyeth Incorporated, Philadelphia. Two teaspoonfuls of the latter contains 4.0 mg. of niacin, 1.2 mg. of vitamin B (thiamine), and 0.5 mg. of vitamin B_2 (riboflavin).

The 137 patients were graded according to the severity of the disease as follows: 4.4 per cent, class 1; 29.2 per cent, class 2; 65.7 per cent, class 3; and 0.7 per cent, class 4.

Table 2 shows the results of treatment in a total of 118 courses of gold administered to 65 patients in the vitamin C and Solganal-B group. Table 3 shows the results obtained in treating 29 patients receiving 66 courses of gold, as well as vitamin B complex. It was observed that patients receiving vitamin B complex reported an improvement in gold is begun, the patient is instructed to pay particular attention to itching, rash and sore mouth. In addition, he is told that any other symptom or sign that may arise should be noted, regardless of severity and regardless of what the patient may think the cause to be. These facts are reported at the next visit and if necessary, treatment with gold is discontinued until the symptom or symptoms disappear. Thus, if a patient reports slight itching for a few hours, treatment is stopped for one week. The appearance of conjunctivitis, simple

TABLE 2. *Result of Treatment, according to Age, in Patients Receiving Gold and Vitamin C.*

Therapeutic Result	Ages							Total Cases	
	Under 20	20–29	30–39	40–49	50–59	60–69	70 and over	No.	Percentage
Group 4 (VMI)	3	2	7	16	21	13	5	67	56.8
Group 3 (MI)	0	4	2	3	4	7	0	20	17.0
Group 2 (I)	0	2	3	5	5	2	0	17	14.4
Group 1 (NI)	0	2	0	1	6	3	1	13	11.0
Worse	0	0	1	0	0	0	0	1	0.8
Totals	3	10	13	25	36	25	6	118	

TABLE 3. *Result of Treatment, according to Age, in Patients Receiving Gold and Vitamin B Complex.*

Therapeutic Result	Ages							Total Cases	
	Under 20	20–29	30–39	40–49	50–59	60–69	70 and over	No.	Percentage
Group 4 (VMI)	3	4	4	8	13	4	0	36	54.5
Group 3 (MI)	0	2	5	3	1	2	0	13	19.7
Group 2 (I)	0	0	1	2	2	2	1	8	12.1
Group 1 (NI)	0	0	0	1	3	3	2	9	13.7
Worse	0	0	0	0	0	0	0	0	00.0
Totals	3	6	10	14	19	11	3	66	

TABLE 4. *Result of Treatment, according to Age, in Patients Receiving Gold Alone.*

Therapeutic Result	Ages							Total Cases	
	Under 20	20–29	30–39	40–49	50–59	60–69	70 and over	No.	Percentage
Group 4 (VMI)	0	0	10	6	8	8	1	33	57.9
Group 3 (MI)	0	0	0	1	7	6	0	14	24.6
Group 2 (I)	0	0	1	1	1	0	1	4	7.0
Group 1 (NI)	0	0	1	1	2	0	1	5	8.8
Worse	0	0	0	1	0	0	0	1	1.7
Totals	0	0	12	10	18	14	3	57	

appetite, and showed a more rapid gain in weight and a tendency toward less fatigue. The results obtained in the control group (patients who received no supportive measures), are shown in Table 4. Forty-three patients received 57 courses of treatment of Solganal-B alone.

As stated in the previous paper, we believed that patients presenting only subjective improvement should not be included among those having favorable results. Therefore, Table 5, summarizing the favorable results, includes only groups 3 and 4. According to these observations, the use of vitamins as an adjunct in the treatment of rheumatoid arthritis with gold is of little if any value.

As stated above, the previous report indicated a comparatively small percentage of untoward reactions. The steps taken to determine such reactions should be explained. When treatment with dryness of the skin, severe headache, dizziness, pain in abdomen or diarrhea, is a good reason for interrupting treatment long enough to attempt to determine the cause.

The above symptoms, unless of reasonable severity, are not included in the category of untoward reactions. This may be one factor in the low incidence of what we consider to be untoward reactions. It is difficult to evaluate these simple symptoms, but many are probably nothing more than what

TABLE 5. *Summary of Favorable Results, according to Type of Treatment.*

Type of Treatment	Group 3	Group 4	Groups 3 and 4
	%	%	%
Gold and vitamin C	17.0	56.8	73.8
Gold and vitamin B complex	19.7	54.5	74.2
Gold alone	24.6	57.9	82.5

one would expect in a patient receiving no medication.

Periodic blood counts and urinalyses were made. Again, we were unable to note any significant changes in the urine, except in 1 case. There were but 3 cases of severe anemia, all requiring transfusions, and when the red-cell counts were normal, treatment was resumed; one of these was fatal.

Table 6 lists the cases having symptoms severe enough to constitute untoward reactions. Eleven occurred during the first course, 8 during the second, 3 during the third, and 1 during the fourth. The incidence according to type of treatment was as follows: vitamin C and gold, 13.6 per cent (16 in 118 courses); vitamin B complex and gold, 6.1 per cent (4 in 66 courses); and gold alone, 5.3 per cent (3 in 57 courses). The over-all incidence was 9.5 per cent (23 in 241 courses). It is obvious that neither vitamin B complex nor vitamin C in fairly large doses influenced the number of untoward reactions encountered in the treatment of rheumatoid arthritis with gold.

TABLE 6. *Untoward Reactions in 137 Patients (241 Courses).*

Vitamin C and Gold	Dose of Gold	Vitamin B Complex and Gold	Dose of Gold	Gold Alone	Dose of Gold
	mg.		mg.		mg.
Course 1 (11 reactions):					
Pruritus	740	Pigmentation of lips	840	Exfoliative dermatitis	240
Pruritus	840	Pruritus	540	Anemia	640
Seborrhea	190	Seborrheic dermatitis	640		
Pruritus with papular eruption	240				
Pruritus	540				
Pruritus	940				
Course 2 (8 reactions):					
Pruritus	840				
Seborrheic dermatitis	240				
Pruritus	940				
Albuminuria	440				
Seborrheic dermatitis	640				
Purpura hemorrhagica (patient died)	990				
Bronchitis	340				
Papular dermatitis	540				
Course 3 (3 reactions):					
Seborrheic dermatitis	440			Gold bronchitis	440
Anemia	540				
Course 4 (1 reaction):					
		Cholecystitis with hepatitis	1040		

To emphasize the importance of caution the following case, the only fatality in the series, is given in some detail.

A. B., an 18-year-old girl, was first seen on June 19, 1943 with a chief complaint of stiffness, soreness and swelling in all the joints of the upper and lower extremities. Three months previously, she had noticed on arising that her hands were stiff. She paid little attention to this, but in a few days there was swelling. Soon the elbows and shoulders were stiff and sore and it became increasingly difficult to do her work as a clerk. Two weeks after the onset of the illness, she was confined to her home. At that time there was also severe pain and swelling in the ankles and knees. The condition was progressing slowly when she was seen by one of us.

Physical examination at that time showed that the joints of the fingers, wrists, elbows, shoulders, knees, ankles, toes and cervical vertebras were involved. There was typical usiform swelling of the fingers and considerable limitation of motion in most of the joints. The hemoglobin was 41 per cent, the red-cell count 2,700,000, the white-cell count 11,700, and the sedimentation rate 145 mm. (Westergren). The patient was admitted to Jefferson Hospital, where she was transfused four times with 500 cc. of whole blood at each transfusion. She was discharged after 2 weeks. At the time of discharge there was little improvement in the condition of the joints, but examination of the blood showed the following: hemoglobin 71 per cent; red-cell count 4,200,000, white-cell count 7,500, and sedimentation rate 145 mm.

The patient suffered considerably from the arthritis, getting little relief from analgesics. She received 10 mg. of Solganal-B Oleosum twice weekly for four doses, 25 mg. twice weekly for four doses, and 50 mg. twice weekly for four doses. With each dose she received 4 units of crude liver extract. At the end of this 6-week period, she developed a stomatitis, but during treatment the improvement in the joints was dramatic. The pain and swelling completely subsided. There remained only slight stiffness, which was particularly manifest in the early hours of the morning before rising. It was originally intended that the patient should receive a full course of gold, but since a stomatitis developed, gold was stopped and crude liver extract in doses of 4 units three times weekly intramuscularly was substituted.

After 2 weeks of treatment with liver extract only, the stomatitis began to improve; however, there was an exacerbation of the joint difficulty. The hemoglobin was 78 per cent, the red-cell count 3,800,000, the white-cell count 7,800, and the platelet count 240,000. During the following 2 weeks the arthritis was as severe as before treatment.

At the end of the 6th week, the stomatitis had disappeared but the arthritis was worse than ever before. The patient and her mother, insisting on resumption of gold therapy, were fully apprised of the serious dangers attendant on such a course. They assumed full responsibility for all eventualities and treatment was resumed with lower dosages. Twenty-five milligrams was administered at weekly intervals from October 18, to April 1, 1944. Four weeks after the new course of treatment was started improvement in the joints was again noted. The improvement continued until March 25, when the patient began to have slight pain in the joints. At that time the hemoglobin was 72 per cent, the red-cell count 3,550,000, the white-cell count 6,200, and the platelet count 260,000. Because of the slight exacerbation of pain it was decided to increase the dose of gold to 50 mg. Up to that point gold had been well tolerated. The following week, the patient presented bleeding from the gums and purpuric spots over the feet and legs. She was admitted to the Philadelphia General Hospital on April 3, with the diagnosis of rheumatoid arthritis and thrombocytopenic purpura due to gold therapy.

While in the hospital, she received fifteen 500-cc. transfusions of whole blood, but the red-cell count never rose above

3,400,000. The platelet count varied, except terminally, from 60,000 to 200,000.

The bleeding from the gums subsided on May 3, but sporadically recurred later in the month, when the purpura had become more generalized. The liver and spleen were palpable below the costal margin.

A biopsy of the sternal bone marrow on June 15 showed abnormal megakaryocytes, and splenectomy was not advised.

On June 30 the patient's condition became alarming. Bleeding from the gums was continual, and the purpura had become generalized. The platelet count dropped to 45,000, the hemoglobin to less than 7.5 gm. per 100 cc., and the red-cell count to 1,500,000. On July 3, there was a massive hematemesis and the patient died suddenly. Permission for an autopsy was not obtained.

Since Forestier[2] in 1929 described the use of gold preparations in the treatment of rheumatoid arthritis, sufficient time has elapsed to permit the establishment of this form of therapy as an important part of the armamentarium for the treatment of this disease. Hundreds of cases have been treated with gold, and thousands of courses of treatment have been completed.

The use of gold preparations in so-called "burnt-out" cases of rheumatoid arthritis, hypertrophic arthritis and the specific arthritides is valueless. One should not delay until all other forms of treatment have failed before instituting treatment with gold. This is an unjustified waste of time during which a patient may continue to have unnecessary discomfort and deformities.

Early acute cases not responding to the removal of foci of infection offer the greatest opportunity. In our cases, attempts were made at removal of these foci of infection. The teeth, tonsils, prostate, cervix, gall bladder and colon were studied. Infection, whenever feasible, was removed or treated. In some cases the arthritis subsided promptly; in others no specific beneficial results were obtained. Our experience indicates that in many cases the judicious removal of all foci of infection within the first three to six months of the onset of the arthritis suffices to bring about a remission, but rheumatoid arthritis of longer duration does not appear to be affected by such treatment. In the latter cases the early institution of gold therapy is justified. The majority of these cases, however, were of long standing.

It is hoped that statistics summarizing the results of treatment of 259 patients, to whom a total of 417 courses of gold injections were administered, may help in evaluating this form of therapy. These statistics (Table 1) are based on the cases in the previous report[1] and those presented in this paper. It is obvious that very marked improvement (Group 4) was obtained in 48 per cent, marked improvement (Grade 3) in 18 per cent and improvement (Grade 2) in 22 per cent; in other words, 88 per cent of the courses appear to have resulted in benefit.

Table 8 gives a summary of the untoward reactions in both series with respect to those occurring in each course. It is clear that the number of untoward reactions was comparatively low. The length of time that it took for the reactions to disappear is interesting. Anemias subsided in a matter of weeks, whereas skin rashes sometimes took many months to disappear. When a generalized pruritus was manifest without a rash, however, it usually disappeared in a few days to two weeks. When the reaction subsided within a few weeks or less, treatment was again started, but the dose was generally limited to 50 mg. weekly. If the reaction reappeared, gold was not used again. Likewise when a severe or a prolonged rash was manifest, the patient was labeled as too sensitive to gold and it was not used again in that case.

TABLE 7. *Results of Gold Therapy in All Cases.*

COURSE	GROUP 4		GROUP 3		GROUP 2		GROUP 1		WORSE	
	NO.	PERCENTAGE	NO.	PERCENTAGE	NO.	PERCENTAGE	NO.	PERCENTAGE	NO.	PERCENTAGE
Course 1	127	49	40	15	65	25	21	8	6	2
Course 2	45	47	19	20	18	19	11	11	3	3
Course 3	15	36	12	29	6	14	9	21	0	0
Course 4	9	53	6	35	1	6	1	6	0	0
Course 5	2	67	0	0	0	0	1	33	0	0
Totals	198		77		90		43		9	
Averages		48		18		22		10		2

At the present time, it is believed that moderate doses of gold (Solganal-B Oleosum), not to exceed 100 mg. per week and a total of 1240 mg. per course are safe. Larger doses carry increased risks; smaller doses do not give so good a result, but our tendency is toward lighter rather than heavier dosage. In our experience, untoward reactions may be manifest early in the treatment, as can be adjudged from Table 6. It has been stated that very small doses are more to be desired.[3] Most cases, however, do not begin to respond to treatment until the dose of 50 mg. is reached. The continuation of this dose suffices provided it is administered twice weekly, but 100 mg. given weekly is more convenient for the patient.*

TABLE 8. *Untoward Reactions.*

	NO. OF CASES	NO. OF REACTIONS	PERCENTAGE OF REACTIONS
Course 1	259	23	8.9
Course 2	96	15	15.6
Course 3	41	4	10.0
Course 4	16	1	6.2
Course 5	5	0	0.0
Totals	417	43	
Average			10.3

*Since these statistics were compiled our policy has been to substitute 50-mg. doses for the 100-mg. doses administered at weekly intervals. This makes a total of 790 instead of 1240 mg. for a complete course.

In respect to sedimentatiom rates, the previous paper[1] showed that they returned to normal in only 7.3 per cent of the cases. The whole group of 259 cases shows that in 8.1 per cent of those receiving 1 course of gold, 7.3 per cent of those receiving 2 courses and 14.3 per cent of those receiving 3 courses, the sedimentation rates returned to normal. In those cases that did not return to normal after 3 courses, the sedimentation rate remained rapid even after 4 or 5 courses.

Gold is not usually administered to patients who have a normal sedimentation rate; occasionally, however, one encounters a case that responds to no other treatment, and in desperation one uses gold. Such has been the case with 9 of our patients. Of these, 4 showed excellent results and 2 were decidedly improved. One was unimproved, and 2 showed only subjective improvement. It appears, therefore, that withholding this drug from patients because the sedimentation rate is normal is not always justified. One should not hasten to use gold, however, when the sedimentation rate is normal. It should be employed only as a last resort. There were no untoward reactions in this group.

The sedimentation rates were reduced in 72.9 per cent of cases given the first course of treatment. In 35.5 per cent the rate was reduced only moderately, whereas in 37.4 per cent it was reduced by 50 per cent or more.

Thirty-three cases (12.7 per cent) showed an increase in the sedimentation rate following a single course of treatment. Fourteen were very much improved, and 5 were much improved. Thus, 19 patients showed both subjective and objective improvement in spite of an increase in sedimentation rate. Thirty-five patients showed an increase in sedimentation rate following 2 courses. Of these, 21 were both subjectively and objectively improved. Eleven cases likewise showed an increase in sedimentation rate following 3 courses, 6 patients being improved. In 7 cases the rate was increased after 4 courses, and 6 patients showed similar improvement. Although it is true that the reduction in sedimentation rate indicates favorable progress, it is also true that an increasing sedimentation rate does not always mean unfavorable progression of the disease.

It is curious that there is obvious objective improvement and apparent freedom from discomfort in these cases, yet the sedimentation rate remains rapid. We are continuing to keep a goodly number of these patients under observation to determine whether the improvement is temporary and whether the sedimentation rate is as important as we think it to be at present.

The arthritis clinics at Jefferson Medical College and Philadelphia General hospitals have been active fifteen and nineteen years, respectively. In retrospect, it is with a great deal of satisfaction that we are able to make this report. For years we have stood by and observed our patients progress from an early rheumatoid arthritis to permanent invalidism. We have removed foci of infection and have used vaccines and bacterial filtrates, both subcutaneously and intravenously, sulfur, chemicals, analgesics, physiotherapy, bee venom, snake venom, vitamins and so forth. Occasionally the effects obtained appeared encouraging; however, after continuation of one form of therapy or another a stalemate was reached. Gold therapy, on the other hand, has given us a new hope for these sufferers. We have been working with gold compounds for about five years, and consider that of all the drugs used, none have been so promising. It is true that we are not in a position to call our patients cured. There are many, however, in whom the condition has remained apparently arrested for a few years.

We are attempting to follow our cases and hope soon to report on the progress made by them. This is difficult, especially when dealing with ambulatory cases. It may be that some day more may be learned about the etiology of rheumatoid arthritis and that a specific remedy may be found. Until that day arrives, it is our opinion that gold therapy judiciously used offers the best therapeutic approach.

Summary

Two hundred and fifty-nine patients with rheumatoid arthritis have been treated with from 1 to 5 courses of gold in the form of Solganal-B Oleosum, for a total of 417 courses.

The giving of 300 mg. ascorbic acid daily did not aid in the reduction of untoward reactions in 65 patients receiving 118 courses of gold.

Vitamin B complex was not a factor in reducing untoward reactions in 29 patients receiving 66 courses.

The percentage of improvement was no greater in the groups receiving vitamins as an adjunct than it was in the group of 43 patients receiving 57 courses of gold alone.

One fatality due to thrombocytopenia purpura is reported in detail. Because of objective improvement in 88 per cent of the various courses of treatment, gold preparations are recommended for the treatment of rheumatoid arthritis, but extreme caution must be exercised.

A normal sedimentation rate is not always a contraindication to gold therapy.

An increasing sedimentation rate during treatment is not always an indication that clinical improvement is not to be expected.

There were untoward reactions in 10.3 per cent of 417 courses of treatment; however, there were untoward reactions in only 8.9 per cent of 259 patients receiving a single course of gold. In the 96 patients receiving 2 courses of gold, the percentage of untoward reactions rose to 15.6 per cent.

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ACTIVE IMMUNIZATION AGAINST SCARLET FEVER*

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THERE are a substantial number of physicians who are opposed to active immunization against scarlet fever, claiming that the accompanying reactions are unusually severe. The presence of this opposition, despite the fact that such immunization has been shown to be effective,[1–3] is thought provoking, and for this reason, a report is presented of the reactions in 377 private patients actively immunized against scarlet fever during the last thirteen years.

The purpose of this paper is to describe a method of active immunization against scarlet fever through use of graduated doses of scarlet-fever streptococcus toxin that was found effective both in completely immunizing against scarlet fever and in minimizing the frequency and severity of the reactions and to furnish an analysis of the resultant reactions in 340 children.

PROCEDURE

Nine patients were immunized in 1933 according to the method suggested by Dick.[4] Five weekly injections of 250 units, 2000 units, 8000 units, 25,000 and 80,000 units, respectively, were given to each child. The series of injections was preceded and followed by a Dick test. Because of the frequency — 21 of the 45 injections were followed by a general reaction — and severity of the reactions, however, and because 4 of the patients had positive Dick tests at the end of the series, an attempt was made to increase more gradually the number of units of toxin given before reaching the final dose.

Twenty-eight patients were divided into three groups during 1933 and 1934 and immunized by means of six, seven and eight injections, respectively, given at one-week, two-week and three-week intervals. It was soon determined that the most effective method with the lowest incidence of general reactions, was that of seven consecutive weekly injections, and that method was employed in immunizing 340 children in subsequent years.

The injections were given subcutaneously in the following doses: 650 units, 2500 units, 5000 units, 10,000 units, 25,000 units, 55,000 units and 110,000 units, a total of 208,150 units. If a moderate or severe general reaction occurred, the same dose was repeated the following week. In case of an allergic reaction, the injections were stopped. Immunization was conducted during the spring or fall, preference being given to the late spring. This was done because respiratory infections are less frequent then than at other times, which obviated the tendency of parents to blame the injections for all the infections and ailments that might develop independent of immunization.

The patient was permitted his usual regime. Recent upper respiratory infections and a history of allergic sensitivity in the patient or in the family were noted. The mother was instructed to note the reactions, both local and general. Local reactions were considered those that involved redness and tenderness at the site of the injection; general reactions included nausea and vomiting, fever, rash, itching, malaise, marked fatigue, irritability, muscular stiffness, nasal hemorrhages, pallor, cold sweats and headaches — alone or in any combination.

Immunization was confined to children over one year of age. The Dick test was given before and after the series of injections during 1935 to 1944, inclusive. If the subsequent test was positive, another series of injections was immediately begun. In the group of 72 children immunized during 1945, the Dick test was not done in the pre-school group and it was used only to test for immunity before the series of injections were given in the others.

The reactions following the seven weekly injections were carefully studied. Since local reactions rarely caused concern to the parents, only the general reactions were analyzed with reference to frequency, type, age and a history of allergic sensitivity in the patient or the family.

A special study was made of 27 children who were immunized against scarlet fever during April and May, 1939, and of 71 patients similarly immunized during the same period in 1944. All these children were immunized just after an epidemic of upper respiratory infection due to a hemolytic streptococcus had occurred in the community. A study was also made of 10 children who had been in direct contact with a case of scarlet fever just previous to immunization.

RESULTS

The general reactions were comparatively infrequent (Table 1). Of 2357 injections given, only 166 (7 per cent) produced general reactions. The most frequent of these was nausea and vomiting, rarely accompanied by diarrhea or abdominal pain; it occurred 91 times (Table 2). The children were pale, perspired freely and vomited, usually from one to three times, although some patients vomited as many as nine times. Most of these reactions

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occurred two or three hours after immunization. An elevated temperature was present 40 times, a rash 12, and fatigue 7. Four children had allergic reactions, and muscle pains were noted 4 times.

TABLE 1. *Relation of General Reactions to Injections.*

INJECTION	DOSE UNITS	NO. OF INJECTIONS	GENERAL REACTIONS NO.	GENERAL REACTIONS PERCENTAGE
First	650	340	21	6.2
Second	2,500	339	36	10.6
Third	5,000	336	33	9.8
Fourth	10,000	336	26	7.7
Fifth	25,000	335	16	4.8
Sixth	55,000	334	18	5.4
Seventh	110,000	334	16	4.8
Eighth (repeat)		3	0	0.0
Totals		2357	166	
General average				7.0

One child developed nasal bleeding thirty-six hours after 4 of 8 injections. Itching of the skin occurred in 2 children; headache resulted in 1, and swelling

TABLE 2. *Type of General Reaction Following Immunization.*

TYPE OF REACTION	NO. OF REACTIONS	PERCENTAGE OF TOTAL
Nausea and vomiting	91	54.8
Elevation of temperature	40	24.1
Rash	12	7.2
Fatigue	7	4.2
Muscle pain or lameness	4	2.4
Nasal bleeding	4	2.4
Allergic reaction	4	2.4
Itching of skin	2	1.2
Headache	1	0.6
Swelling of axillary lymph nodes	1	0.6

of the axillary lymph nodes in 1. In 28 children there was more than one reaction.

Total immunity to the scarlatinal toxin of the hemolytic streptococcus was apparently afforded in practically every case. After completing the series of injections, only 3 of the entire series of 268 patients immunized prior to 1945 had a positive Dick test, thus requiring a second series of injections. Furthermore, no case of scarlet fever has developed among these children.

The percentage of general reactions during immunization was lowest (4.7) in the youngest patients, those between the ages of one and two (Table 3). The highest rate (17.0 per cent) occurred in those

TABLE 3. *Relation of General Reactions to Age.*

AGE YR.	NO. OF CHILDREN	NO. OF INJECTIONS	GENERAL REACTIONS NO.	GENERAL REACTIONS PERCENTAGE
1	181	1267	59	4.7
2	56	394	35	8.9
3	35	245	29	11.4
4	15	105	9	8.6
5	15	103	8	7.8
6	13	88	15	17.0
7 to 11	25	155	11	7.1
Totals	340	2357	166	

between six and seven years old, and the next highest (11.4 per cent) in those between three and four. The rates in the other age groups ranged from 7.1 to 8.9 per cent.

In April and May of 1939 and 1944 there was present in the vicinity of Boston a mild epidemic of upper respiratory infection due to different strains of hemolytic streptococcus. Fifteen of the 98 patients immunized at these times had a general reaction following the first injection.

Of the 10 children who had been in close contact with a scarlet-fever patient just previous to immunization, 2 had general reactions after the first injection, 5 had unusually marked local reactions, consisting of redness and swelling of the upper arm about the site of the injection, and 3 had no unusual general or local reaction.

There were 140 children who had a family or personal history of allergic sensitivity. Of these only 4 developed allergic reactions during immunization. The reactions consisted of swelling of the face, including the eyelids, nose and lips, and of the tongue, dyspnea and a maculopapular rash (2 children). In 1 child the reaction followed the first injection, and in 3 it followed the second.

DISCUSSION

The peak of positive Dick reactions in children is between the ages of one and two years, being over 90 per cent, and the incidence of general reactions during scarlet-fever immunization is lower at this age level than at any other. Because of the high percentage of positive Dick reactions in preschool children, Bacon[5] suggests that all children of this age be assumed to be susceptible to scarlet fever and that active immunization follow as a matter of routine, as is customary in diphtheria immunization. This suggestion was followed in the 72 children in this series immunized in 1945.

There was an interesting similarity between the percentage of general reactions in the 98 children immunized during the epidemics of 1939 and 1944 and that in the 10 children actively immunized after having been in direct contact with scarlet-fever patients. In the first series the percentage was 15, whereas in the second series it was 20. The similarity would be even more striking, 18 as compared with 20 per cent, if 3 children not included among the former are added. These children, aged one, two and four years, respectively, were given the first injection following a recent upper respiratory infection, one of them in 1939 and the other two in 1944. They developed a local reaction, with rectal temperatures of 101 to 103° F. The parents refused further immunization. In these 108 children there were seventeen general reactions following the first injection, as compared with only four general reactions following the corresponding injection in the remaining 232 children.

These reactions were not due to the presence of a nonspecific upper respiratory infection for in the spring of 1945 there was a widespread upper respiratory infection in the community. Of 72 children immunized, 31 had upper respiratory infections; however, only three general reactions followed the first immunizing dose. This suggests

that when hemolytic streptococcus infection is present in the community, a higher proportion of persons than usual are sensitive to the initial immunizing dose of scarlet-fever toxin. The work of Lancefield[6] and Griffith,[7] who by a precipitation reaction and an agglutination technic proved the existence of many different serologic types of streptococci associated with human infection, is pertinent in this respect. All these types may be associated with typical scarlet fever, some much more frequently than others. These same types have also been isolated from cases of septic sore throat, tonsillitis, erysipelas, otitis media and other nonscarlatinal infections.

None of the 10 children immunized after exposure to scarlet fever developed the disease. Although this suggests that the immunity response in susceptible children when given a single dose of scarlet-fever toxin after contact with the disease is rapid enough to prevent infection, such a thing seems unlikely in view of the short incubation time of the disease and the appreciable time usually required for the development of immunity.

A history of allergic sensitivity does not preclude immunization against scarlet fever in children, as shown by the fact that only 4 of the 140 patients with such a history developed an allergic reaction. Apparently the procedure of choice is to immunize routinely irrespective of sensitivity, but to stop the immunization if an allergic reaction occurs following an injection.

The reactions described in this paper may have been due either to the direct toxic action of the immunizing agent or to hypersensitiveness to some constituent of it — perhaps a nucleoprotein.

Although it was impossible to gather adequate comparative statistics, the impression was gained that the nonscarlatinal hemolytic streptococcus infections that occurred among the immunized patients were less both in frequency and in severity than they would have been without immunization.

Summary and Conclusion

A modified method for active immunization against scarlet fever is described. Seven weekly injections are given, which result in fewer general reactions and a higher degree of immunity than are obtained following the usual Dick method.

The incidence of general reactions was 7 per cent among 340 children between one and twelve years of age immunized during the last eleven years. The most frequent general reaction was nausea and vomiting.

Ten scarlet-fever contacts and 98 children actively immunized during epidemics of upper respiratory streptococcal infections had high incidences of general reactions — 20 and 15 per cent, respectively — following the first immunizing dose.

Immunity, as evidenced by a negative Dick test, was complete in 98.9 per cent of the children, a repeat injection being given to the others. With such a high percentage of immunity, a follow-up Dick test is probably unnecessary.

None of the 340 patients developed scarlet fever.

The best age to immunize actively for scarlet fever is between one and two years. The incidence of general reactions was lowest in this group. Since there is a scarlet-fever susceptibility of over 90 per cent at this age, an initial Dick test is not necessary.

A history of allergic sensitivity is not a contraindication to immunization.

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CLINICAL NOTE

SPONTANEOUS RUPTURE OF A NORMAL SPLEEN

Report of a Case

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ALTHOUGH it is difficult to accept the idea that the normal spleen can rupture under normal physiologic conditions, a relatively small number of cases of seemingly proved authenticity have been reported in the surgical literature during the last twenty years.

There are various theories adopted to substantiate spontaneous rupture of the spleen. Susman[1] has summed up the process of spontaneous rupture as follows: softening of all structures of the spleen; congestion of the portal vein and its radicles and inability of the narrower splenic vein to accommodate itself, blood thus being forced between the spleen and investing peritoneum, which finally gives way; and perisplenic adhesions, which by fixing the organ predisposes to rupture. Byford[2] in reporting a case stated his belief that the spleen was not normal in its entirety and that the rupture occurred at a localized diseased area, which was destroyed by the hemorrhage resulting from the rupture. Rhame[3] believed that the engorgement of the spleen with blood during digestion might predispose to rupture. Zuckerman and Jacobi[4] reported 20 cases of spontaneous splenic rupture. Many reported cases show disease of the gastrointestinal tract, especially of the gall bladder. Roettig et al.[5] hold that these cases represent instances of delayed rupture, the history of trauma being overlooked, and that there may be latent periods as long as six months before rupture occurs in a previously traumatized spleen.

Spontaneous rupture of the pathologic spleen is not infrequent and has been reported from in cases of typhoid fever, leukemia, malaria, hemophilia and pregnancy. Such a case during the last trimester of pregnancy was reported to me shortly after the following case occurred.

S. C. (J. H. 30095), a 28-year-old, married woman, entered the Jordan Hospital on March 9, 1944. The night before admission she was awakened by sharp pains in the upper abdomen, which interfered with breathing. The pains were not localized. She had to sit up to catch her breath, and on doing so felt cold and sweaty. Soon after this she fainted while moving her bowels; this apparently resulted in no injury. After being revived she breathed more easily but she could not move on account of the persistent upper abdominal pain. A few hours after the onset of the pain she noted pain in both shoulders. There was no nausea or vomiting. The bowels were regular. There were no urinary or other gastrointestinal symptoms. The regular menstrual period began on this day, without dysmenorrhea.

The past history was essentially negative. A normal delivery had occurred about 2 years previously.

Physical examination showed a well developed and well nourished woman, with a pallid skin and complaining of abdominal pain. The temperature was 100.6°F. The examination was otherwise negative except for the abdomen, which was doughy and spastic throughout, especially in the left upper quadrant. There was diffuse pelvic tenderness on vaginal examination. No masses were palpable. The consulting gynecologist, Dr. M. O. Belson, thought that there was active intraperitoneal bleeding, probably secondary to ectopic pregnancy.

The patient was given 1 unit of plasma and prepared for laparotomy. Under ether anesthesia a low midline incision was made. There was considerable free blood in the lower abdomen and pelvis. Careful survey of the uterus, tubes and ovaries was negative. There was no bleeding from the broad ligaments. There was an ecchymotic area subperitoneally near the uterine end of the left sacrouterine ligament. This was opened and inspected, but no active bleeding was noted. It was apparent that the pelvis and pelvic organs were not responsible for the bleeding. The cecum and lower ileum and the liver were normal. On palpating the spleen it was obvious that the source of bleeding was coming from a rent in the convex surface near the upper pole.

By that time the patient was in a critical condition from loss of blood, the exploratory palpation having aggravated the bleeding. The lower incision was extended upward to the left costal margin, all clots were removed, and a splenectomy was rapidly performed, only the splenic pedicle requiring ligature. The lower incision was closed in layers; the upper incision was closed with single through-and-through cotton sutures. A rubber drain was placed in the left gutter near the splenic bed. Owing to the pulpy softness of the spleen and the haste necessary to complete the operation on account of the patient's condition, the spleen was traumatized during removal.

At the close of the operation the patient was moribund, cold and pulseless; the blood pressure was not obtainable. A vein was exposed in the antecubital fossa and 1500 cc. of citrated blood and 2 units of plasma were given, with good improvement.

The postoperative course was fairly uneventful. The temperature rose to 103°F. the day following operation and fluctuated up to 101°F. for 1 week, after which it remained normal. The wounds healed without infection. The patient received intravenous sulfadiazine, vitamin K, ferrous sulfate and liver extract during convalescence. The blood picture before discharge showed a mild secondary anemia.

The spleen was examined in the Leary Laboratory, with the following report:

> The specimen consists of a spleen weighing 340 gm. and measuring 15 by 10 by 4 cm.* On the diaphragmatic lumbar surface there are multiple lacerations, two of the largest being situated one on either pole. The latter are jagged and measure roughly 6 cm. in length. They appear to lift up the flaps of tissue. There is a small linear superficial longtitudinal tear 6 cm. in length in the midportion of this surface, and a deep incised laceration along one of the lateral borders extending inward 4 cm. The hilar surface presents many irregularities, with an excavation 5 by 4 by 1 cm. It is probable that this excavation represents the effects of operative trauma, and the incised and longtitudinal lacerations may be similar defects. From their appearance the polar lacerations on the diaphragmatic and lumbar surfaces may well have been the result of preoperative trauma.
>
> On section the capsule is extremely thin, and the cortex is nodular, red-brown and extremely pulpy, with indistinct follicles and trabeculae. Microscopically the section demonstrates the usual splenic architecture, with well formed follicles and distinct sinusoids and trabeculae. There is evidence of hemorrhage in the traumatized areas.
>
> Diagnosis: ruptured spleen.

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*It is appreciated that the spleen weighed nearly twice as much as the generally accepted limit of normal. On the other hand, the reason for the increase in weight was not evident from microscopic examination, nor has the patient subsequently developed a condition, such as leukemia, that might have accounted for the splenic enlargement.

SUMMARY

A case of rupture of the spleen is reported in which there had been no history of trauma, either recent or remote, in a previously well woman.

I am indebted to Dr. F. J. Abate for the opportunity to report this case.

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MEDICAL PROGRESS

PRACTICAL ASPECTS OF OXALATE METABOLISM*

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THERE are a wide variety of substances involved in human nutrition. The extensive literature dealing with the more important ones — vitamins, proteins, iron, glucose and so forth — tends to overshadow the modest literature concerning a wide range of less known and often less important substances of nutritional significance. As a result, many physicians fail to give them even the limited attention they deserve. Therefore, it is well periodically to re-emphasize subjects that are in general poorly understood.

Many common foods contain organic acids. Citric, malic, oxalic, tartaric, benzoic, lactic, isocitric, malonic, succinic, aconitic, tricarballylic, salicylic, quinic and glyoxylic acids are representative organic acids found in foods. These vary widely not only in the amount and frequency of occurrence in various foods but likewise in their nutritional and metabolic significance for human beings. The papers by Smith and Orten[1] and by Mattice[2] may be consulted for a general discussion of this subject. Smith and Orten concisely state the problem in these words:

> The presence of a number of the organic acids in mammalian tissues and body fluids has been repeatedly demonstrated. Questions therefore arise regarding the origin, possible effects and ultimate fate of these substances in the organism. Obviously, they may be derived from the preformed acids in ingested food. However, there is convincing evidence that certain acids are endogenous in origin and that they may be formed in the course of the metabolism of the carbohydrates, fats or proteins. Also, there are increasing indications that certain organic acids are not fortuitous constituents of living matter but that they are involved in definite physiological processes.

It is the purpose of this report to discuss one of these, namely, oxalic acid, which is a dicarboxylic acid with the formula HOOC=COOH-2H$_2$O. There is a considerable but widely scattered literature, chiefly in German, French, Italian and English. Our interest in this acid was stimulated several years ago while studying a forty-three-year-old woman who had repeated attacks of oxaluria with renal colic and hematuria, with persistence of this syndrome in spite of the use of a low-oxalate diet.

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OXALIC ACID CONTENT OF FOOD AND ITS RELATION TO THE AVAILABILITY OF CALCIUM

Oxalic acid is present in many foods. This represents the exogenous source of part of the blood and urine oxalates normally present in man. Table 1 gives data on the oxalic acid content for some representative foodstuffs, compiled from different sources.[3–7] For more detailed information and for values for other foods these original sources can be consulted. The analyses by Kohman[7] are the most modern and extensive. These reported values are of help to the physician in enabling him to prescribe a diet low in oxalic acid if it appears indicated for therapeutic purposes.

It is apparent that oxalic acid is widely distributed among the common foodstuffs. Chocolate, cocoa, tea and certain vegetables contain relatively large amounts, whereas fruits, meats and certain other foods contain little or frequently none. Of the vegetables, on the basis of Kohman's determinations, spinach, Swiss chard, New Zealand spinach, beet tops, lamb's quarters, poke, purslane and rhubarb have high contents. In contrast, peas, cucumbers, radishes, cauliflower, squash and turnip contain no oxalic acid. Most vegetables range between these two extremes.

Because the leafy vegetables serve as a valuable source of dietary calcium, much interest has been shown in the study of the effect of oxalates on the availability of calcium. In view of the prominence given by nutritionists as well as by comic-strip artists to the ingestion of spinach, it is not surprising that much of the research has been centered around this vegetable.

Most reports[5–15] agree that the oxalic acid content of spinach (*Spinacea oralacea*) and New Zealand

spinach (*Tetragonia expansa*) is high, often 10 per cent of the dried substance. The oxalate is present primarily in the form of insoluble calcium oxalate crystals, which can be demonstrated in microscopic sections of the leaves. The calcium content also is high. It has been estimated,[14] however, that the oxalate content of spinach is sufficient not only to make unavailable its own calcium but also to precipitate an equal amount of calcium supplied by other foods in the diet.

TABLE 1. *Oxalate Content of Common Foodstuffs (Expressed as Percentage of Oxalic Acid).*

Food	Esbach[3]	Arbenz[4]	Widmark[5]	Majumdar and De[6]	Kohman[7]
	%	%	%	%	%
Vegetables:					
Beets (leaves)	—	—	—	—	0.916
Spinach	0.191–0.327	0.29	0.837	0.658	0.892
Spinach, New Zealand	—	—	—	—	0.890
Swiss chard	—	—	—	—	0.645
Rhubarb (stalks)	0.247	0.32	0.396–0.511	1.336	0.500
Sorrel	0.274–0.363	0.27	1.772–2.263	—	—
Beets	—	0.03	—	0.0404	0.138
Potatoes, sweet	—	—	—	—	0.056
Beans, wax	0.0312	0.045	0.039	—	0.041
Celery (stalks)	0.0025	Trace	—	—	0.034
Carrots	0.0027	—	0.016	0.0056	0.033
Endive	0.0045	0.003	—	—	0.0273
Onions	0	0.005	0.055	0.001	0.023
Turnips (leaves)	—	—	—	—	0.0146
Kale	—	—	—	—	0.013
Escarole	0.0017	—	—	—	0.0116
Peas	0	—	0.036	0.006	0
Beans, lima	0.0158	—	—	—	0.0043
Asparagus	0	0.009	0	—	0.0052
Broccoli	0	—	—	—	0.0054
Cabbage	0	—	0.010	0.0059–0.0185	0.0077
Brussels sprouts	0.002	0.004	—	—	—
Corn	Trace	—	—	—	0.0014
Lettuce	0	—	0	0.0136	0.0071
Potatoes, white	0.0046	0.04	0	0.015	0.0057
Squash	—	—	0.007	—	0
Cauliflower	—	0.006	0	0.0068	0
Cucumbers	0	—	0	—	0
Fruits:					
Gooseberries	—	—	0.027	—	0.088
Raspberries, black	0.0062	0.05	—	—	0.053
Grapes	0	—	—	—	0.025
Oranges	0.003	0.01	0.028	—	0.024
Currants	0.013	0.03	0.066–0.072	—	0.019
Strawberries	0.0012	—	0.020	—	0.019
Blackberries	—	—	—	—	0.018
Blueberries	—	—	0.044	—	0.015
Raspberries, red	0.0062	—	0.042	—	0.015
Apricots	Trace	—	—	—	0.014
Plums	0.007	Trace	0	—	0.010
Prunes	0.012	—	—	—	0.0058
Bananas	—	—	—	—	0.0064
Peaches	Trace	Trace	—	—	0–0.0050
Pears	0	0.02	0	—	0.0030
Pineapples	—	—	—	0.0058	0.0063
Tomatoes	0.0002–0.0052	0.008	0	0.0036	0.0075
Apples	Trace	Trace	0	—	0
Grapefruit	—	—	—	0.0034	0
Lemons (juice)	0.003	Trace	0.033	—	0
Melons	0	0.003	—	—	0
Miscellaneous:					
Tea, black (dry)	0.375	1.43	1.386	0.2192	—
Cocoa	0.352	0.48	0.645	0.442	—
Chocolate	0.09	—	—	—	—
Coffee	—	0.08	0.043	0.0154	—
Wheat, flour	0	Trace	0	0.0111	—
Rye, flour	0	—	0	—	—
Corn meal	—	0	—	0.0099	—
Rice	0	0	—	0.0046	—
Bread, white	0.0047	—	—	—	—
Beef	—	—	0.025	—	—
Milk	—	—	0.0019	—	—
Mutton	—	—	0.0069	—	—

Experiments on rats have shown that the calcium in pure calcium oxalate supplied orally is not utilizable.[7,15] Soluble oxalates added to the diet interfere with the utilization of calcium carbonate[16] or of

calcium supplied in skim milk[17, 18] as a result of the formation of the insoluble calcium salt. Numerous investigators[7, 10, 11, 14–17] have demonstrated that when spinach provides the calcium content of the diet to varying degrees, calcium retention is markedly less than in similar experiments in which the source is skim milk or one of the vegetables with low oxalate content. Growth is depressed,[7, 14] the animals appear weak and unkempt,[11] mortality is increased,[7] bone and tooth development is impaired,[7] and reproduction is unsuccessful.[7] MacKenzie and McCollum,[19] on the other hand, demonstrated that in the rat if potassium oxalate is added to an adequate diet no deleterious effects result unless the oxalate concentration is 2.5 per cent or a simultaneous deficiency of vitamin D, calcium or phosphorus occurs.

Nutritional studies on man have not been so numerous. Interest in the literature has centered chiefly in the oxalic acid content of foods and its possible adverse influence on calcium metabolism. Edelstein et al.[12] report that the calcium of spinach is poorly utilized by young infants. Bonner et al.[20] in a well controlled experiment showed that the addition of 100 gm. of puréed spinach or its equivalent in oxalic acid to the daily dietary of 10 growing children caused no significant variations in the nitrogen, calcium or phosphorus utilization. No toxic effects were noted during the period of the experiment. Similar findings have been reported in adults.[13]

It seems, therefore, that under conditions of certain animal experiments the calcium of spinach is nonavailable for bodily utilization and that this is related, at least in part, to the oxalic acid content of the spinach.

The Council on Foods of the American Medical Association[13] in a detailed report on the nutritional value of spinach, summarizes its conclusions on this point as follows:

> Metabolism experiments show that the feeding of spinach is of no value during early infancy as a source of calcium; there is of course, plenty of calcium in milk to meet the needs of normal infants. The evidence also shows that in young children and in adults receiving diets adequate in calcium content the inclusion of spinach does not adversely affect the calcium metabolism.

This is therefore a reasonable and practical view for the physician to take.

Toxicology

Oxalic acid is an example of a toxic substance that is consumed with impunity in small amounts in the daily food, yet when ingested in large amounts in pure form causes serious illness or death. It has considerable toxicologic interest. Knowledge of the oxalates is said[21] to date from the middle of the seventeenth century, at which time Duclos mentioned that "salt of sorrel," or potassium oxalate, could be obtained from the plant *Oxalis acetosella*. In 1773, Savary obtained oxalic acid from the potassium salt. In 1776, Bergmann obtained "acid of sugar" by oxidation of glucose with strong nitric acid, and this was subsequently shown by Scheele to be identical with the acid obtained from the plant oxalis. Oxalic acid has had various household and industrial uses, such as bleaching of cloth and straw, dyeing and calico printing, cleaning of leather and woodwork, scouring of brass and copper and removing of ink stains. It can be readily purchased in a drugstore and is widely used in industry. Druggists are required to keep a record of sales.

An acute illness or even fatal poisoning[21, 22–29] may follow the ingestion of oxalic acid or one of the soluble oxalates. Because of their extremely sour taste these substances are seldom used in cases of homicide, but they may be ingested accidentally or with suicidal intent. Their close superficial resemblance to Epsom salts has been responsible for many cases of accidental poisoning, and their availability as household bleaching and cleansing agents has made them occasional mediums for attempted suicide.

Acute poisoning is much more frequent than is chronic. Only a few cases of the latter have been reported, and it is therefore poorly understood. Hamilton[27] reviews 2 interesting cases. The first, described by Grolnick in 1929, was that of a painter who intermittently for a period of two years used oxalic acid in cleaning floors without protecting his hands with rubber gloves. He experienced severe pain, stiffness and numbness of the fingers. Examination revealed deep cyanosis involving the fingers and hands to the wrists; the soft tissues were tense; the skin felt cold, and the nails were yellow in color. Recovery followed treatment with hot Epsom salt soaks, dry heat and woolen bandages. The second case was reported in 1939 by Howard.[30] This was the case of a man whose occupation involved the cleaning of automobile radiators. In this work he boiled parts in a strong solution of oxalic acid and consequently for a period of several months was heavily exposed to oxalic acid fumes. In addition, he frequently handled oxalic acid crystals with his bare hands. His symptoms were referable to the respiratory, gastrointestinal and central nervous systems. There were a metallic taste in the mouth, marked irritation of the eyes and throat, frequent epistaxes, severe headaches, repeated vomiting, persistent cough, productive at times of fragments of tissue, melena, severe low-back pain, loss of weight, muscular weakness and albuminuria. Recovery was slow, and a state of extreme nervousness persisted for a long period.

Acute poisoning develops within a few minutes to several hours after the ingestion of oxalate. The range of the lethal doses is extremely wide, values between 2 and 30 gm. of oxalic acid having been reported. Death is undoubtedly a result not

only of the quantity of acid consumed but also of other factors, such as the form in which the oxalate is consumed, the interval between consumption and therapy, the type of treatment, the condition of the patient prior to ingestion, the renal status and the gastric acidity. Death has occurred as early as three minutes and as late as fourteen days after ingestion. The symptoms of acute toxicity may be divided into those caused by a local corrosive action and those resulting from absorption and excretion of the soluble oxalate. If a high concentration or the solid form is taken, the local effects may be predominant and death may occur without development of symptoms dependent on absorption. Immediately on ingestion there is noted an extremely sour taste, followed by a violent sensation of burning in the mouth, pharynx and region of the stomach. There may be marked dysphagia and a sense of constriction in the throat. Within a few minutes retching and vomiting occur; the vomitus is described as being coffee-ground in color or dark red. Vomiting may become intractable and be followed by severe diarrhea, with or without melena. If the condition is untreated, the vomiting and diarrhea persist and the patient may die from dehydration and exhaustion.

If death does not result from collapse associated with acute hemorrhagic gastroenteritis, symptoms develop from the systemic effects and from renal insufficiency. The former are related to the depressing action of oxalate on the blood calcium,[24] by which it is rendered nonavailable, and possibly to some direct toxic effect on tissue cells.

It has been estimated that approximately 0.6 gm. of oxalic acid in the human blood stream at one time is equivalent to the blood calcium.[8] The cardiovascular, neuromuscular and central nervous systems are markedly affected. The skin is pale, cold and clammy, the pulse is weak or imperceptible, and the blood pressure and temperature are low. Numbness and tingling may develop in the extremities. Cramplike muscular and abdominal pain may be extremely severe. An erythematous rash has been noted. Local or generalized muscular twitchings occur and may progress to marked tetany and convulsive seizures. The tetany of oxalic acid poisoning is due to acute calcium deficiency and can be relieved by the intravenous administration of calcium salts. The central nervous system may show evidence of excitation or depression varying from an acute maniacal state to stupor and coma. Death results from cardiovascular collapse or depression of the central nervous system.

Renal involvement is frequent and, even if the patient survives the severe local and systemic effects, may be responsible for a fatal outcome. Renal insufficiency dominates the picture from the second day.[31] Oliguria develops and may progress to anuria. The blood nonprotein nitrogen rapidly rises. Examination of the urine shows albuminuria, numerous epithelial cells, hyaline and epithelial-cell casts, erythrocytes and calcium oxalate crystals. If anuria does not develop, oliguria is followed by polyuria and hyposthenuria, which may persist for a long period. If anuria occurs early or the onset of polyuria is delayed, the prognosis is poor.

The treatment of oxalic acid poisoning consists of repeated gastric lavage with lime water, intravenous calcium gluconate or chloride and supportive therapy directed toward maintenance of the fluid balance, an adequate renal output and a normal blood pressure.

Acute oxalic acid poisoning has been reproduced experimentally in animals. MacKenzie and McCollum[19] in rats, Rost[31] and Heubner and Hückel[32] in dogs and Baudouin et al.[33, 34] in rabbits and dogs have duplicated the sequence of events that occurs in cases of human poisoning. The depression of blood calcium has been verified,[34–36] and some evidence has been obtained that the severity of the reaction is controlled in part by the parathyroid glands.[36]

Considerable attention has been focused on the pathologic lesions developing in the kidneys of animals used in experiments involving acute and chronic oxalic acid poisoning. Dunn et al.[37] reviewed the literature and reported their own results in rabbits. The severity and reversibility of the damage varied with the amount of oxalate injected. The kidneys were swollen, pale and edematous. Marked necrosis, especially of the proximal convoluted tubules, occurred. Although occlusion of some of the renal tubules by calcium oxalate crystals was noted, this did not appear to be an essential feature of the nephritis. Gough[38] studied the mitochondria of the renal tubular epithelial cells and was able to demonstrate by his technic that even quantities of oxalic acid well below toxic doses cause cellular changes, which, however, were reversible. On the other hand, as the dose is increased nonreversible necrotic changes develop, which are detectable by ordinary histologic procedures. Most authors[33–39] agree that the glomeruli are unaffected but that the epithelial cells of the convoluted tubules become swollen and necrotic. Calcium oxalate crystals have been demonstrated within the lumens of the renal tubules as well as within the epithelial cells. Heubner and Hückel[32] noted that at autopsy the kidneys showed the largest oxalate content of any organ and that examination of tissue sections by means of polarized light showed a wide distribution of crystals throughout the kidney. Koch[34] in a study of the kidneys of a fatal human case also was able to demonstrate intracellular oxalate crystals. Attempts to produce macroscopic oxalate calculi have not been highly successful. Rost,[31] however, reported oxalate concretions in the calyces of the kidneys of three dogs fed sodium oxalate for several months and Keyser[40, 41] was able on a few occasions to produce renal calculi in rabbits after

the administration of large amounts of butyl oxalate with calcium chloride or oxamide.

Koch[24] concluded from his experiments that the type of renal damage depends on a number of variables, the most important of which is the nature of the oxalate excreted. Thus, if sufficient oxalic acid or soluble oxalate reaches the kidney a necrotizing nephritis may result, whereas if absorption has been slow and sufficient time has elapsed for complete combination with calcium, the results depend on the hypersecretion of a normal urinary constituent.

Rhubarb Poisoning

From time to time there have appeared in the medical literature references to episodes of acute illness following the ingestion of rhubarb, particularly the leaves, and certain other foods — for example, sorrel.[42–50] The knowledge that such foodstuffs have a high oxalic acid content has invariably led to the incrimination of oxalic acid as the toxic factor in these cases. For instance, Widmark and Ahldin[5] report that the stalks of rhubarb plants contain 0.39 to 0.51 per cent oxalic acid, whereas the leaves contain only 1.2 per cent. Other authors report comparable values.

Beattie,[51] in this country, in a government pamphlet issued in 1937, discussed this problem in these words:

> The succulent acid leafstalks of rhubarb make most excellent sauces and pies, and the question often arises about the use of the leaf blades for greens. Numerous cases of more or less serious illness and some fatalities have been reported in both Europe and in North America from eating rhubarb leaves. These leaf blades were eaten boiled in the belief that they were a suitable substitute for the common greens, but *owing to the high content of oxalic acid and its soluble salts found in rhubarb leaves it is recommended that they be left entirely alone and not used under any circumstances as food.* In the stalks, however, the oxalic acid is present in smaller amount and largely in insoluble form, and for this reason is harmless.

This subject has also, in recent years, received editorial comment in the *Journal of the American Medical Association.*[52]

As reported in the literature the symptoms of rhubarb poisoning varied greatly. In mild cases the symptoms are those of a gastroenteritis, with abdominal pain, vomiting — occasionally with hematemesis — and diarrhea predominating. In severer cases, hemorrhagic diathesis, dysuria, hematuria, convulsions, collapse, noncoagulability of the blood and coma have been noted. At times, genitourinary symptoms — renal colic with hematuria — without gastrointestinal manifestations have been observed.

Almost all the reported cases are in the earlier literature. Many occurred in England during World War I, at which time it had been suggested by various newspapers that rhubarb leaves be used as a vegetable substitute. The role of oxalic acid in some of the reported cases of rhubarb poisoning is open to question. At times the amount of rhubarb consumed scarcely seemed likely to contain enough oxalic acid to be poisonous. Kohman[8] refers to an investigation by Maue in which he and five other men repeatedly ingested cooked rhubarb leaves with no toxic effects whatsoever. Other reports indicate that a food rich in oxalic acid was responsible for death or illness.[50] In one case death occurred after ingestion of half a peck of cooked rhubarb leaves and part of the water in which it had been cooked.[50] On investigation of an outbreak of "ptomaine poisoning" following the ingestion of soup of sour grass (sorrel), a public-health official found that the soup contained about 0.13 per cent oxalic acid. The precise minimal amount of oxalic acid necessary to produce symptoms is not known, and perhaps varies with individual susceptibility and gastric acidity.

It is well to remember that the gastroenteritis of food infection may readily simulate mild oxalic acid poisoning, and conversely that the abdominal pain, vomiting and diarrhea due to the ingestion of oxalic acid may simulate the gastroenteritis or gastritis of food infection. Since some skepticism has been expressed about this subject, physicians who encounter suspected cases of rhubarb poisoning could make a worth-while contribution to the medical literature by reporting cases that have been carefully studied by modern chemical and bacteriologic methods. There is a distinct paucity of reliable information on this subject in the modern literature.

It is known that ingestion of an ordinary portion of cooked rhubarb stalks may cause an increase in the urinary excretion of oxalate.[53] In a susceptible person this may occasionally be the contributing factor in the production of clinically significant oxaluria. There are a number of reports of hematuria attributed to the ingestion of rhubarb.[47, 48]

The Syndrome of Oxaluria and Oxalemia

The identification of crystals of calcium oxalate in the urine by Donné in 1838 stimulated interest in their clinical significance. Within the following decade attempts were made to correlate the presence of the crystals with the occurrence of definite symptoms and signs, and under the influence of Prout, Golding Bird and Begbie,[54] there emerged the concept of a so-called "oxalic acid diathesis." Subsequently an extensive literature developed and such terms as "syndrome of oxaluria," "oxalemia," "oxalic acid diathesis" and "oxalic gout" became diagnostic scrap baskets. The German literature is conspicuous for the paucity of reports on this subject. A few papers have appeared in the English and American journals, but the greatest source of information has been the work of French and Italian investigators, who, it would seem, have been unduly influenced at times by the great European spas.

The terms "oxalemia" and "oxaluria" refer to a state in which the oxalic acid levels of the blood and urine respectively are elevated above normal. Such elevated values have been reported in a wide variety of diseases, for example, diabetes, acute and chronic renal insufficiency, cirrhosis of the liver, nutritional deficiencies and cardiac failure. In addition to these well-recognized clinical conditions, oxalemia and oxaluria are said to be found in association with a variety of symptoms and signs that, grouped together, have been considered as a specific syndrome. The variations in the manifestations of this syndrome are numerous. It may mimic an acute abdominal crisis or biliary or renal colic; it simulates gastrointestinal or genitourinary disease; it presents itself as a disease of the muscles or joints; or it manifests itself as a disease of the central nervous system.

Neville[55] and Goiffon and Nepveux[56] refer to a constitutional diathesis associated with the syndrome. The patient is irritable, depressed, anxious, hypochondriacal, dyspeptic and neurasthenic. In addition, he may show periodically one or any combination of the following clinical pictures.

The gastrointestinal tract may be, and frequently is, the site of greatest disturbance.[57–60] There may be epigastric distress after eating, diarrhea alternating with constipation, severe gastric crises with retching, vomiting, even hematemesis and spasmodic intestinal pain, which may be accompanied by the passage of calculi or blood from the rectum. The vomitus has been reported to contain calcium oxalate crystals.[57] The abdominal pain may be extremely severe and associated with signs of an acute intestinal obstruction. A description of 2 such cases, one of which was subjected to abdominal exploration, was reported by Rawling.[61] These, however, appear to have been cases of oxalate lithiasis with marked gastrointestinal symptoms and need not be designated as a special syndrome.

A second manifestation of the syndrome is renal in nature. The literature contains a number of reports of severe renal episodes thought to be examples of the syndrome.[62–71] In general, the picture is that of severe renal colic, either unilateral or bilateral. There is pain in the flank, which may radiate to the genitalia, frequency, urgency, burning on urination, cystalgia and gross and microscopic hematuria. Reflex gastrointestinal symptoms — vomiting, abdominal distention and so forth — may occur. The episodes are paroxysmal and at times appear to have a tendency toward a seasonal recurrence, being most prominent during the summer. In some reports this has been attributed to the consumption of such foods as rhubarb, spinach, tomatoes, strawberries and gooseberries, foods thought to be rich in oxalates; others attribute it to the precipitation of calcium oxalate crystals because of concentration of the urine during the warm weather. Most of the reported assays, however, fail to confirm high oxalate values in any but the first two mentioned foods. Examination of the urine at the time of the attacks reveals a heavy concentration of calcium oxalate crystals, irritation from which is the explanation for the pain and hematuria. Roentgen-ray and cystoscopic examinations have been negative in the cases in which studies have been made. The symptoms are said to disappear when the patient is maintained on a low oxalate diet and fluids are forced. The renal manifestations of the syndrome appear to be the best substantiated. The most modern support to the theory that oxaluria may produce symptoms has been given by Black.[63] Oxaluria with symptoms — chiefly colic and hematuria — occurred in 43 men and was the most frequent urologic condition requiring hospital admission among soldiers from a British division training in India. In this study oxaluria was not diagnosed until a full investigation — cytologic and bacteriologic examination of the urine, cystoscopy and intravenous or retrograde pyelography — had been carried out to exclude other causes for these symptoms. Black also presented some cases suggesting that oxaluria with epididymitis may be a distinct entity.

Loeper,[72] Loeper et al.[73] and Violle[59] use the term "oxalic acid gout" to designate a condition in which the oxaluric diathesis is accompanied by symptoms and signs associated with the muscles or joints. They claim that patients with this ailment have oxalemia with a variety of findings, for example, migraine headaches, psychasthenic depression, vague pains, hypotension, gastric and intestinal crises, mucous colitis, intestinal and renal lithiasis and hematuria. In addition, they have severe chronic rheumatism and arthritis and may develop a tophaceous type of "gout." The rheumatism is described as an afebrile, slowly progressive, chronic disease. There are vague pains in the extremities and fingers, with crepitation of the knees and shoulders. Enlargement of the ends of the phalangeal bones occurs, and knotty deformities the size of lentils may develop on the lateral aspects. Sometimes mild dislocations occur. On roentgenologic examination the bones appear to be rarefied, and there is thickening of the periarticular tissues, deformities of the phalanges and erosions of the ends of the bones. The tophi, when present, are aberrant, juxta-articular or articular in location. It is thought that originally the tophi are primarily pure calcium oxalate, but that eventually they change to calcium carbonate or are followed by the precipitation of cholesterol and uric acid so that mixed tophi result. Loeper[72] claims that the administration to a patient of this type of calcium oxalate or foods rich in oxalates causes an exacerbation of the symptoms.

Grott[74] reported 4 cases of acute arthritis clinically indistinguishable from acute gouty arthritis. When the patients failed to respond to the routine therapy for gout, determinations of blood uric acid

and oxalic acid showed the former to be normal and the latter elevated. Clinical improvement followed administration of diets low in oxalates. Dietary indiscretions were frequently followed by exacerbations of symptoms. Grott concluded that some cases of gouty arthritis are related to disturbances in oxalic acid metabolism rather than to those in uric acid metabolism. This concept has not been confirmed.

Cohen and Reid[75] reported 7 cases of tenosynovitis crepitans involving the flexor and extensor tendons of the wrist. Although it was true that in most cases mechanical strain appeared to be a precipitating factor, oxaluria occurred in every case, and in 3 cases there was in addition a history of urinary lithiasis. There was no response to the usual therapy until a regime of low-oxalate diet, alkalinization and increased intake of magnesium was instituted.

Laroche[76] has summarized the clinical picture of oxalemia with involvement of the central nervous system. Asthenia, melancholia and vague pains have been noted. Migraine attacks are frequent. Intercostal, crural, sciatic and brachial neuralgia may predominate. Convulsive seizures have been reported by Rodillon[77] in patients whose spinal fluids contained crystals of oxalic acid. Finck[78] reported the case of a patient with severe headache and the signs of marked meningeal irritation. The condition persisted until the onset of hematuria associated with marked oxaluria, following which the neurologic picture completely disappeared.

In its complete form this syndrome apparently mimics a wide variety of clinical pictures. The mechanisms suggested to explain it are largely speculative and, except for the renal phase, remain for the most part as obscure as the so-called "facts" related to the intermediary metabolism of oxalates.

The syndrome of oxaluria with colic and hematuria is often mentioned in the American literature and in textbooks on urology. There appears to be a growing appreciation of the fact that renal colic and hematuria may result from the passage of crystals or microscopic aggregates of crystals as well as from macroscopic stones. For example, sulfonamide therapy may give rise to it. Less known but well described in the literature is the syndrome of uric acid showers with renal colic.[79–81] Uric acid crystals may precipitate out, irritating the renal pelvis and ureter and producing colic. They redissolve before voiding. The patient passes very acid urine, generally clear of crystals but containing red blood cells. If the urine is allowed to stand for twenty-four to seventy-two hours in a sterile test tube, crystals precipitate on the glass and on tapping the tube rain to the bottom and may be collected for microscopic and chemical analysis.

A large municipal hospital like the Boston City Hospital receives many emergency admissions for renal colic. We have been impressed over the years with the frequency with which the standard K.U.B. (kidneys, ureters and bladder) roentgenogram and routine pyelogram, when used alone, fail to demonstrate a calculus or to establish the cause of the colic. It is well for the physician to keep in mind that the clinical picture of renal colic without a demonstrable calculus on a K.U.B. roentgenogram may be due to a non-shadow-producing calculus or mass, — uric acid, fibrin or blood clot, — Dietl's crisis, sulfonamide lithiasis, oxaluria, syndrome of uric acid showers, possibly the passage of excessively concentrated urine and so forth. Patients admitted to a hospital for renal colic should be instructed to void each specimen of urine into a urinal through a piece of cloth. Not only does the recovery of some gravel or a stone establish the diagnosis, but chemical analysis indicates the nature of the calculus and enables the physician to plan a more rational method of therapy. Urine voided during or shortly after an attack of colic should be examined for crystals as well as other sediment, the specific gravity and the pH. Red blood cells disappear if urine stands too long or is too dilute. If the urine is extremely acid a specimen in a sterile test tube should be set aside for precipitation of uric acid crystals. A chemical test for cystinuria, the Sulkowitch test for hypercalcinuria and culture of urine for urea-splitting organisms are well within the scope of any hospital laboratory. These procedures often enable the cause of renal colic to be established when calculi are not detected by roentgen-ray study.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31331

PRESENTATION OF CASE

A fifty-nine-year-old woman was admitted to the hospital complaining of a mass in the abdomen.

Ten months before admission the patient noticed, after reaching forward, a sensation of heaviness in the abdomen occurring about once a month and followed on one occasion by watery diarrhea. Four months later, while lying on her right side, she detected a mass in the left flank that progressively increased in size but caused no symptoms, except a sensation of weight; at times it seemed to pulsate. Two months before admission she had an attack of low back pain, which radiated upward and was severer than the back pains that she had had for many years. During this period she worked hard and became weak, tired and dyspneic; after a period of rest these symptoms disappeared.

The past history was noncontributory except that she had been jaundiced for one month thirty years previous to admission.

On examination the patient was a well developed, moderately obese woman in no acute discomfort. Multiple subcutaneous nodules were palpable over the arms and thighs. The heart and lungs were normal. In the left upper quadrant of the abdomen was a firm, moderately tender, irregular mass about 10 cm. in diameter. It descended with inspiration and was movable on pressure in the left costovertebral angle. Peristaltic sounds were heard in the region of the mass. Pelvic and rectal examinations were negative.

The temperature, pulse and respirations were normal. The blood pressure was 125 systolic, 80 diastolic.

Blood examination showed 14.9 gm. of hemoglobin and a white-cell count of 7400. The stools were negative for occult blood. The nonprotein nitrogen was 15 mg. per 100 cc., and the fasting blood sugar 100 mg. The total serum protein was 6.1 gm. per 100 cc. The serum amylase was 36 units per 100 cc. All urine specimens were negative.

A barium enema done ten days before admission showed passage of barium from rectum to cecum without delay. There was reflux into a normal appearing terminal ileum. No constant filling defect, ulceration or diverticulum was seen in the colon. The ascending colon and cecum were twisted on themselves so that the tip of the cecum lay in essentially the same position as the hepatic flexure. The palpable mass in the left upper quadrant was not attached to the bowel (Fig. 1). It displaced the splenic flexure laterally, and the transverse colon inferiorly. The palpable mass was distinctly seen on the film. It measured 10 cm. in diameter. The stomach appeared to lie medially to the mass and above it. The spleen was not visualized. A small-bowel enema showed the mass to lie in the left upper quadrant, between the stomach and transverse colon, displacing the stomach upward and the transverse colon and upper small intestine downward. An intravenous pyelogram was negative. A gastrointestinal series was negative.

On the ninth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. MERRILL C. SOSMAN†: I should like to have more details about the nodules found over the arms and thighs. How large were they? Were they freely movable? What was their distribution? Was there any pigmentation associated with them? I assume that they were neurofibromas.

DR. BENJAMIN CASTLEMAN: There is no further information recorded. I should agree that they were probably neurofibromas.

DR. SOSMAN: "The heart and lungs were normal." I assume that statement was based on the usual method of examination with the stethoscope, which is not reliable in spite of what one of your doctors said at one of these meetings several months ago.‡ Since there are no x-ray films of the chest, we must accept the opinion, but not as a fact.

The serum amylase was 36 units per 100 cc. At the Peter Bent Brigham Hospital anything up to 100 units is normal. This was well below the border line of abnormality.

Submitted with this protocol was this series of x-ray films. There are several facts that can be determined from the x-ray studies, and opinions can be deduced from these facts. I think that we should carefully separate the two. First there is a barium enema, then a small-bowel study, then intravenous urograms, and finally, a gastrointestinal series. I was a little intrigued in going over these films to find that all of them have the same identifying number but one. I assume that you have a unit number for these patients, and I wonder if this film belongs to the group.

DR. DEAN CRYSTAL: The patient was seen in the Out Patient Department and given a number, and was then transferred to the house and given another

*On leave of absence.

†Clinical professor of radiology, Harvard Medical School; radiologist, Peter Bent Brigham Hospital.

‡Case records of the Massachusetts General Hospital (Case 31122). *New Eng. J. Med.* 232:353-358, 1945.

number before it was realized that she was the same patient.

DR. SOSMAN: We can check that statement by observing the details of the spine — the intimate, personal, private anatomic details. As a matter of fact, x-ray films are a good method of identifying persons during life and even after death, and they have frequently been used for that purpose. If one compares the transverse processes, the articular facets upward. There is a large vacant area here, which spreads the duodenal loop. It looks as if the mass had moved to the right side. I cannot tie that up with the examination when it was said that the mass was in the left upper quadrant. I should like to ask if the mass moved.

DR. LAURENCE L. ROBBINS: Dr. H. P. Mueller, who did the fluoroscopy, — in fact, I believe that he interpreted all the films, — was certain that each

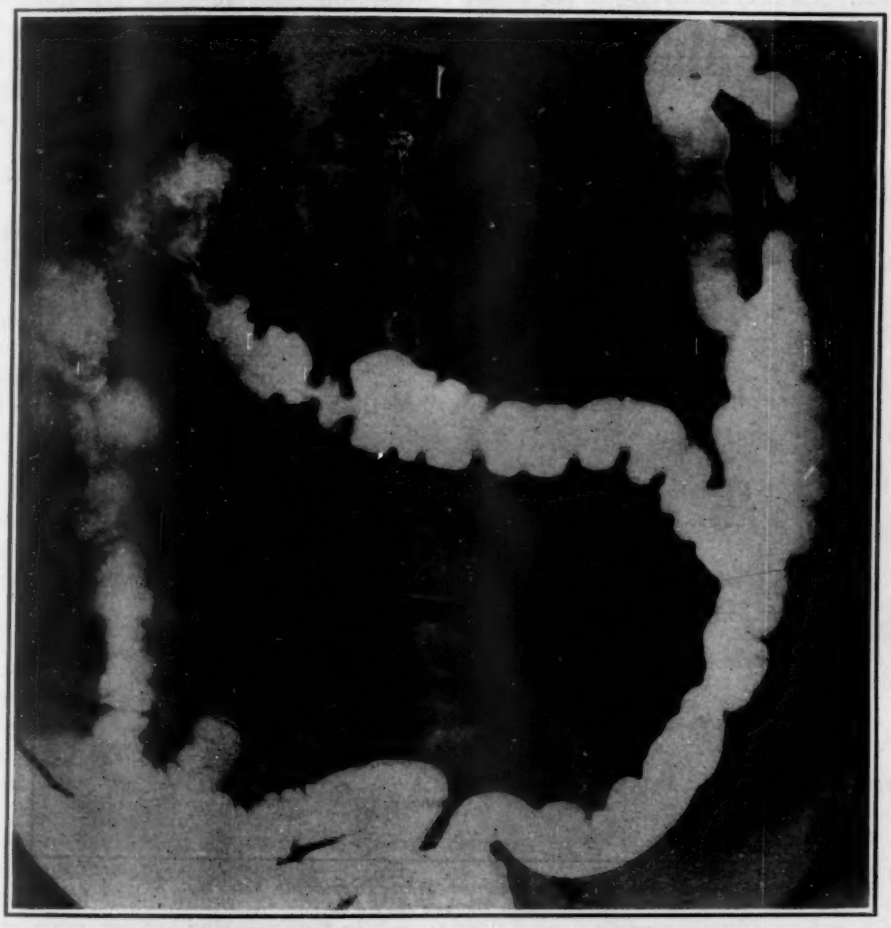

FIGURE 1. *Roentgenogram of the Abdomen Showing the Soft-Tissue Mass in the Left Upper Quadrant.*

and the details of the fourth and fifth lumbar verbras in these films one finds that they are identical, so that the statement is correct.

The outline of the mass is best seen in this film of the kidney and bladder region, which preceded the intravenous urogram. There is a fairly sharply outlined mass in the left upper quadrant, which also shows well in the barium-enema film. The protocol states that the mass was irregular to palpation, whereas the shadow on the x-ray film is smooth and distinct in outline, making it look like a cystic mass. I agree, however, with the report that the first barium enema was normal. There is no evidence that the tumor arose from the colon. The stomach is displaced time he examined the patient the mass was in a different part of the abdomen.

DR. SOSMAN: So it was a freely movable mass, and I assume that the mass in the right upper quadrant below the antrum of the stomach, lying above the colon and distending the duodenal loop (Fig. 2), is the same one that we saw in the left upper quadrant (Fig. 1).

The intravenous urogram is essentially normal, except that the upper calyxes of the left kidney are not well filled. There are two small areas of calcification that might be interpreted as the tips of these calyxes, since they are in proper relation to the outline of the kidney. As a matter of fact, the

two shadows are present in the plain film before the intravenous urogram was made. I assume that these two small calcified areas were in the mass and were not part of the kidney.

Finally the gastrointestinal series shows a well filled stomach, with normal mucosa and normal peristaltic waves, and a normal duodenal loop. I consider this jejunal loop to be abnormal. It is a little too large, and the rugae on the left side adjacent to the mass are not entirely distinct. Going back to the small-bowel examination, I see a loop of small bowel that I think is larger than one ordinarily sees.

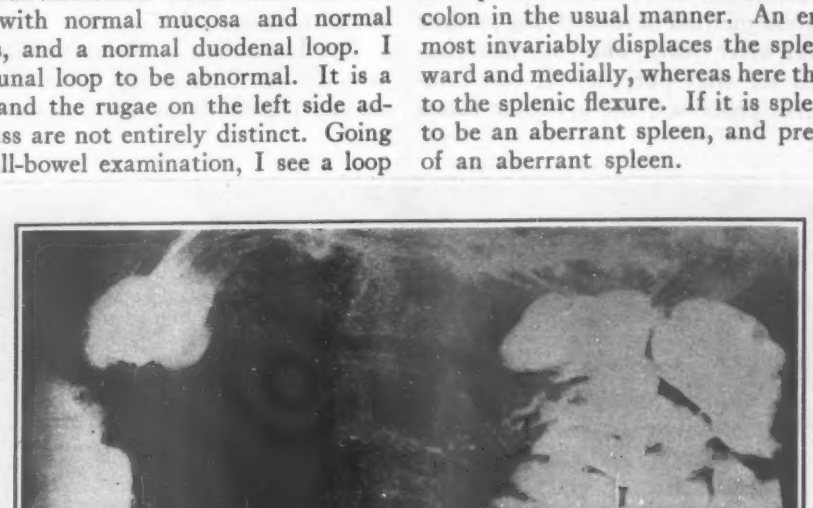

FIGURE 2. *Roentgenogram Showing the Mass Displacing both the Barium-Filled Stomach and the Colon.*
The mass has migrated to the right of the spine.

To sum the whole thing up, the patient came in with a mass in the left upper quadrant, and after nine days of hospital study the diagnosis was still a mass in the left upper quadrant. I do not believe that there is any evidence here to indicate the exact origin of the mass. From these examinations, however, we do know that it was not a part of the stomach and that it did not arise from the colon; if this dilated loop of small bowel means anything, it could have arisen from the wall of ileum. We have to consider, then, a tumor of the small bowel, a mesenteric cyst, a tumor of the left kidney (with no more distortion of the renal pelvis than we have here, it would probably have to be a large benign cyst), a cyst in the tail of the pancreas and, finally, an ovarian cyst with a long pedicle. These are the five major considerations. I believe that we can rule out the spleen because the tumor does not displace the colon in the usual manner. An enlarged spleen almost invariably displaces the splenic flexure downward and medially, whereas here the mass lies medial to the splenic flexure. If it is spleen, it would have to be an aberrant spleen, and presumably a tumor of an aberrant spleen.

Going back to the small bowel and jejunum, there are four or five conditions that are commonly found there. One is reduplication, which almost always is found in children. I believe that it is quite rare to see it in a woman of fifty-nine. Then there are the sarcomas, — leiomyosarcoma and spindle-cell tumors, — but in such cases there is almost invariably a history of ulceration and hemorrhage. This patient had no anemia and no blood in the stools. The episode of weakness, fatigue and dyspnea could have indicated a massive gastrointestinal hemorrhage, but she failed to notice tarry stools. Lymphoma is frequently found in the small bowel, but that also is likely to cause hemorrhage, although not so often as the spindle-cell sarcoma; further-

more, there is usually evidence of the disease elsewhere. Finally, we must consider a neurofibroma arising in the wall of the bowel or one of the nerves in the mesentery. She had subcutaneous neurofibromas, but I do not remember ever having seen a large neurofibroma in the abdomen. This is still a possibility in spite of that.

Mesenteric cysts are fairly rare. A cyst of unknown etiology with chylous fluid or serous fluid is occasionally seen. And there are the so-called "enteric cysts"; the pathologists give them this name, but they are probably the same as the reduplications that they talk about at the Children's Hospital. There are also the extremely rare nephrogenic cysts, which occur in the bowel remnants of the wolffian body, and a dermoid cyst, not associated with the ovary, is occasionally found. In fact, the two areas of calcification are suggestive of the latter.

I do not believe that it was a cyst of the pancreas because it was so freely movable and because of its location. It could have been a cyst of the ovary with a long pedicle, and that might account for the severe attack of pain in the back radiating upward, assuming that the previous ones that she had had many times were from the same cause. That would nicely explain the pains — torsion of an ovarian cyst with a long pedicle.

After looking over all these possibilities, I have no particular opinion concerning what it really was. I have ruled out a good many things, but there are still some even more remote possibilities, such as carcinoid of the small bowel or argentaffin tumors. These are found in association with multiple neurofibromas, but the carcinoid or argentaffin tumor is extremely small and rarely undergoes cystic degeneration; in all probability it can be ruled out. I have narrowed the field down to two main possibilities — ovarian cyst with a long pedicle and enteric cyst in the wall of the small bowel. Ovarian cyst must be considered, particularly because of the remarkable mobility of the mass. I believe that we can rule out cyst of the kidney. If this is the same tumor on the right, we can rule out cyst of the pancreas. I shall have to make a double-barreled diagnosis, so to speak, instead of pinning all my faith on a single one, that is, enteric cyst or ovarian cyst.

Dr. Robbins: We followed the same line of reasoning as Dr. Sosman. I do not believe that we were impressed with the appearance of the jejunum. Dr. Mueller said that during fluoroscopy the jejunum appeared to be normal. I thought that it probably was a cyst in the gastrocolic ligament because of the way it so consistently maintained its relation to the colon and stomach.

Clinical Diagnosis

Pancreatic cyst.

Dr. Sosman's Diagnosis

Enteric or ovarian cyst.

Anatomical Diagnosis

Multilocular cystoma of pancreas.

Pathological Discussion

Dr. Castleman: Dr. Crystal, will you tell us what you found at operation?

Dr. Crystal: We found a large tumor with a granular surface pushing the gastrocolic ligament forward. It proved to be a huge multilocular tumor of the neck of the pancreas, the portion that lies to the left of the notch for the mesenteric vessels. A small part of the mass was attached to the region just to the left of the mesenteric vessels. It could not be dissected free from the pancreas, and yet it appeared to be an encapsulated benign tumor. It was possible to transect the pancreas in two places, one just to the left of the uncinate notch and the other just to the left of the tumor, at a distance of about 5 cm., and to lift the tumor out, preserving intact the splenic vessels, which we did not have to tie. The question then rose whether or not we should remove the tail of the pancreas and the spleen along with the tumor. We elected to leave the pancreas and spleen; the latter was done because of our observation on several occasions that incidental removal of the spleen has been followed by thrombosis of the splenic vein.

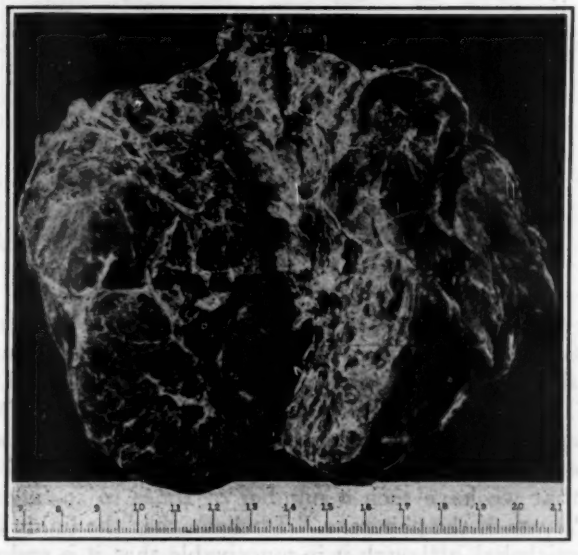

Figure 3. *Photograph of a Cross Section of the Specimen.*

The patient has done well. I do not know whether she will develop a pancreatic fistula. She has had fever every day, and I imagine that a fistula may eventually appear, possibly lasting for several months.

Dr. Castleman: The mass that we received was well encapsulated and quite nodular, but the nodules were smooth, not granular such as one may

see in ovarian carcinoma. These nodular areas were translucent, pinkish and gelatinous, being quite similar in appearance to the thyroid tissue. A cross section of the tumor revealed varying sized multilocular cysts filled with viscid gelatinous semisolid material resembling colloid (Fig. 3).

Histologically one section showed a bit of pancreatic tissue separated from the tumor by a thick

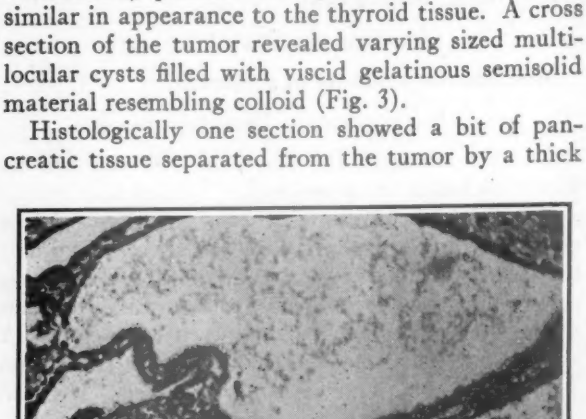

FIGURE 4. *Photomicrograph Showing the Cystic Spaces.*

capsule. The mass was made up of cysts of varying sizes, separated by fibrous connective tissue (Fig. 4). The lining of these cysts was flat to low cuboidal epithelium, and occasionally there was a suggestion of papillary projections. This is the appearance that we have seen a number of times in so-called "cysts of the pancreas." I believe that the lining is epithelial, although it is conceivable that it is endothelial, the tumor being a form of lymphangioma. Although they are often called "cystadenomas," I prefer the term "cystoma" because they really do not form glands. They are simply spaces with single layers of epithelium, occasionally high and with a papillary arrangement. There was no evidence of malignancy.

CASE 31332

PRESENTATION OF CASE

A forty-nine-year-old woman was admitted to the hospital complaining of dyspnea and a sensation of pressure over the sternum.

During the year before admission the patient had had a marked decrease in appetite and had lost 20 pounds in weight. During the same period her teeth had rapidly become carious. Six months before entry she first noted swelling of the ankles and feet, worse at night and accompanied by aching from the hips downward. Exertional dyspnea soon developed, and she became easily fatigued. Early in her illness she complained of pain in the shoulders and arms, usually on the right but sometimes on the left. She consulted a physician, who found albumin in the urine. At that time the red-cell count was 5,000,000. Weakness and fatigue progressed, and she became extremely pale. The red-cell count was found to have decreased to 2,000,000. Liver and iron were given, with improvement of the pallor but not of strength. For nine weeks before admission she was confined to bed. Each evening there was a low-grade fever, the highest temperature recorded being 101°F. Chest plates taken two months before admission were said to have shown healed tuberculous lesions in both lung fields. Two days before admission the patient first experienced an attack of breathlessness, with a sensation of extreme sternal pressure from the xiphoid to the sternal notch, tickling in the throat and a dry spasmodic nonproductive cough, accentuated in the sitting position. There was no chest pain. These symptoms persisted, and respiration was difficult. Orthopnea appeared, with palpitation and sweating. She could not sleep well, and sedatives had been given.

Before the onset of her illness the patient's health had been excellent. One brother had died of tuberculosis, and another brother and a sister had active tuberculosis at the time of the patient's admission.

Physical examination revealed a markedly pale, acutely ill, apprehensive woman, gasping for breath. Purplish blotches were seen about the wrists and ankles. The pupils and fundi were normal. The teeth were markedly carious, with pyorrhea. The tongue was smooth, with no lesions. The cervical, axillary and inguinal nodes were firm, shotty and nontender. The thoracic cage was poorly developed, and the xiphoid depressed. Breathing was chiefly abdominal, without lag or retraction. Over the right upper chest, posteriorly, tenderness was elicited and expiratory wheezes were heard. The mediastinum was widened, extending 1.5 cm. on each side of the midline. The point of maximum cardiac impulse was 8 cm. to the left of the midline. A harsh systolic murmur was heard over the entire precordium. The abdomen was spastic. The edge of the liver was percussed four fingerbreadths below the right costal margin, but satisfactory palpation was impossible. The spleen could not be felt. The reflexes were physiologic.

The temperature was 100°F., the pulse 100, and the respirations 25. The blood pressure was 210 systolic, 100 diastolic.

Examination of the blood showed a red-cell count of 2,090,000, with 5.1 gm. of hemoglobin, and a white-cell count of 13,100, with 85 per cent neutrophils, 7 per cent lymphocytes, 5 per cent monocytes and 3 per cent basophils.

X-ray examination of the chest showed an extensive old tuberculous process; there were mottled areas of increased density and interspersed fibrosis occupying the upper two thirds of both lung fields and

extending into the right lower lung. There seemed to be a cavity in the right upper chest, and probably many small areas of cavitation in both upper lobes, the so-called "bronchiectatic changes" of long-standing tuberculosis. The remaining, better ventilated portions of the lung showed a hazy increase in density.

The temperature varied from 100 to 101.5°F., falling to 97 terminally. The patient went downhill rapidly and expired on the third hospital day.

Differential Diagnosis

Dr. William W. Beckman: There are probably two unrelated parts to this illness — first, the pulmonary disease, which was apparent by x-ray examination, and second, the remainder of the illness: the debility, the edema, the albuminuria, the rapidly progressing refractory anemia, the hypertension and the terminal episode, which is consistent with left ventricular failure in a hypertensive heart. That train of events led me to believe that it was necessary to make a diagnosis of nephritis. The question is what kind of nephritis. One can fairly well rule out malignant hypertension by the fact that the eyegrounds were normal. Between chronic glomerulonephritis and chronic pyelonephritis it is impossible to differentiate without more information regarding the urine than is provided in this protocol. Either might have accounted for the symptoms.

An attractive possibility is periarteritis nodosa, which can, of course, produce nephritis with albuminuria and hypertension, and which would explain some of the other findings that are difficult to account for, such as the skeletal symptoms that she experienced from time to time. These were vague, and I do not know how to interpret them; but vague skeletal symptoms are said to be a feature of periarteritis nodosa. I might say parenthetically that there are two types of periarteritis nodosa: one occurs incidentally along with other conditions, such as hypersensitivity, and the second causes the clinical syndrome of periarteritis nodosa. The latter, which I am incriminating here, is characterized by an insidious onset, with debility, weight loss and symptoms referable to the vascular system. There are vague skeletal pains, as I have said, and also lesions that are compatible with the description of those over the wrists and ankles in this patient. I am afraid, however, that there is not enough evidence here to make a diagnosis of periarteritis nodosa. In the first place, one expects to find eosinophilia, and there was not even a single eosinophil in the blood smear. In the second place, I rather suspect that, if she had died of periarteritis nodosa, she would have had a good many more symptoms referable to the vascular system, such as abdominal pain, pain in the extremities similar to intermittent claudication, cerebral phenomena and so forth. She had none of these, and it is improbable that she had periarteritis nodosa. I say that particularly because every time I discuss one of these cases I make that diagnosis and it is always wrong.

Before I go farther with the discussion I should like to see the x-ray films.

Dr. Milford D. Schulz: The films show what is stated in the protocol.

Dr. Beckman: Undoubtedly, but I do not understand what the protocol said.

Dr. Schulz: The films show fibrous lesions involving the apices. There seems to be something else going on, as shown by the areas of increased density extending from both hilar regions. Several rounded areas of increased density are seen in the lower portions of the lungs. One almost looks as if it had a fluid level.

Dr. Beckman: Could she have had pulmonary infarction?

Dr. Schulz: I wonder if she could have had multiple septic pulmonary emboli in addition to the old disease. The hilar vessels are rather prominent, but there does not seem to be pleural effusion. The heart is enlarged, and there is some prominence in the left auricular area. Calcification in the valves is not apparent.

Dr. Beckman: I still do not know what this patient had. She seems to have had an old pulmonary tuberculosis. I suppose that whether or not this was active cannot be told from the chest films, and in the absence of a sputum examination I cannot decide whether she had an active pulmonary tuberculosis. If it were active, it would account for the low-grade fever that she was running.

If one were to attempt to relate the whole picture, — the pulmonary and the renal disease, — I should think that one would have to bring in the possibility of chronic pulmonary sepsis — tuberculosis or some other disease — leading to amyloidosis, including amyloid kidneys, and thereby causing the train of events that took place. I do not have any way of establishing that diagnosis either, but it is unlikely in view of the high blood pressure, which is not frequent in renal amyloidosis. As a matter of fact, I can mention a lot of things but cannot establish any of them. As I have said, the terminal episode might have been due to left ventricular failure. The abrupt onset of breathlessness is consistent with that. It is rare, however, to have a marked feeling of substernal oppression in that syndrome. Although these patients sometimes complain of precordial discomfort, what this patient experienced is more than usual, and I wonder whether she might have had a large pulmonary embolus two days before admission to the hospital, which was the final cause of her death. I do not believe that I can settle any of these questions.

It seems likeliest that this patient had nephritis, either chronic glomerulonephritis or chronic pyelonephritis. There is no way of differentiating these

two, but I will bet on glomerulonephritis, with resulting hypertension and hypertensive heart disease, left ventricular failure and pulmonary edema. She also had an old pulmonary tuberculosis, which was probably inactive.

A PHYSICIAN: Is carcinoma of the lung of common occurrecne in women and is it ever bilateral?

DR. BENJAMIN CASTLEMAN: Primary carcinoma of the lung is more frequent in men than in women, but it certainly does occur in the latter. It is almost always unilateral. When it is bilateral, the lesions on one side are usually metastases from the other side.

Dr. Schulz, do these films suggest carcinoma?

DR. SCHULZ: I do not know how one could rule it out, but it does not have to be primary in the lung.

DR. E. D. MASON: I have never seen anything like the rash on the ankles and wrists. It resembled post-mortem lividity, and we could not explain it. It was hemorrhagic and deep purplish.

DR. REED HARWOOD: If this patient had left ventricular failure, is it not surprising that she did not have more x-ray evidence of pulmonary congestion?

A PHYSICIAN: A large liver is usually associated with right ventricular failure, rather than with left ventricular failure. What explains the large liver?

DR. BECKMAN: I doubt that it was really enlarged. When the liver is described as large in such vague terms, it usually turns out not to be. Dr. Castleman will settle this point later.

CLINICAL DIAGNOSIS

Pulmonary tuberculosis, active.

DR. BECKMAN'S DIAGNOSES

Chronic glomerulonephritis.
Hypertensive heart disease, with left ventricular failure.
Pulmonary edema.
Pulmonary tuberculosis, probably inactive.

ANATOMICAL DIAGNOSES

Subacute glomerulonephritis.
Hemorrhagic pulmonary edema, severe.
Bronchopneumonia.
Cardiac hypertrophy, hypertensive type, slight.
Periarteritis nodosa, focal: bronchial lymph node and pancreas.
Pulmonary tuberculosis, healed, apical.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Autopsy showed a pair of lungs that were quite heavy, being two or three times the normal weight. There were no adhesions or fluid in either pleural cavity. On section we were unable to find any cavities. In the right lung there was an old tuberculous scar surrounded by compensatory emphysema. It is quite possible that this focal emphysema might have produced an x-ray picture simulating a cavity. This scar was the only evidence of tuberculosis that we could find. The rest of the lungs were boggy and soggy, being full of fluid and blood. Every alveolus was filled with either blood or fluid, and some of them contained polymorphonuclear cells. In other words, this was an extremely severe form of hemorrhagic edema, the type that is often seen in patients with renal disease and the type that was recognized roentgenologically a few years ago by Dr. Richard Schatzki,* of our x-ray department.

We did find renal disease. Each kidney weighed about 100 gm., and although the surfaces were smooth, they were studded with petechial hemorrhages. In gross the prosector, Dr. J. P. Kulka, thought that there probably was a nephritis. Microscopically it proved to be subacute glomerulonephritis. It apparently had gone on to the chronic stage, because none of the glomeruli were completely hyalinized and there was no surface granularity. That fits in with the size of the heart, which weighed only 250 gm., although the left wall was slightly hypertrophied.

An interesting incidental finding, which will probably please Dr. Beckman, was the presence of periarteritis in two vessels, one in a hilar lymph node and the other in the pancreas. The kidneys, however, showed no evidence of periarteritis nodosa. I have not been able to find out whether the patient had ever been given sulfonamides, the thought being that it might have been the result of an allergic reaction.

DR. BECKMAN: How large was the liver?

DR. CASTLEMAN: It was within normal limits, weighing 1500 gm.

*Scott, T., Schatzki, R., and Bauer, W. Pulmonary edema: its roentgenologic appearance in acute glomerulonephritis without signs of cardiac failure. *J. A. M. A.* 114:613, 1940.

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A. M. A. PROGRAM

On page 224 is reprinted the platform that was adopted by the Council on Medical Education and Public Relations and the Board of Trustees of the American Medical Association on June 22 and that originally appeared in the July 21 issue of the *Journal of the American Medical Association*.

Undoubtedly this program will do much to clarify the stand of the American Medical Association, and certainly the fulfillment of its principles would accomplish a great deal toward the improvement of medical care. On the other hand, it seems unfortunate that nothing is said regarding the promotion of co-operation and an improved understanding among groups and individuals concerned with the provision of all types of medical care, that the political control or domination of medical practice is not denounced (rather than a plea being made for the "postponement of consideration of revolutionary changes"), that the need for additional and improved hospital facilities, particularly in rural areas, is ignored, that the necessity of providing adequate means for the postgraduate instruction of discharged medical officers and civilian physicians is disregarded, that the opportunities for advancement in the field of industrial medicine are not mentioned and, finally, that the possibilities connected with education of the public in matters pertaining to medicine, other than those concerned with voluntary insurance, are ignored. Anyone who is at all familiar with the activities of the American Medical Association appreciates that all these matters are receiving due attention, and why they were omitted from a statement purporting to present the ideas of the American Medical Association regarding ways and means for improving the health of the Nation is incomprehensible.

It is obvious that the American Medical Association can do little toward attaining the objectives of this platform: in other words, the program is a direct challenge to physicians and to the state agencies — medical societies, hospital associations, departments of health and so forth — that are involved in the provision of medical and hospital care. Much has to be done, and promptly, if Congress is to be convinced that the provisions contained in the Wagner–Murray Bill (S. 1050) are ill advised and unnecessary.

"WHERE THERE IS NO VISION"

After the war is over, according to the fixed beliefs of many people, — beliefs built firmly around their faith in the fulfillment of a personal wish, — many things will come to pass. Permanent peace will brood over the land, certainly so if our global friends and neighbors adopt our views on international matters; we shall return to the goodness of former days, separated in some mysterious manner from their evil; we shall have new radios, with television, wireless telephones so that we can

CONSTRUCTIVE PROGRAM FOR MEDICAL CARE

AMERICAN MEDICAL ASSOCIATION

This platform was adopted by the Council on Medical Service and Public Relations and the Board of Trustees of the American Medical Association on June 22, 1945.

Preamble

The physicians of the United States are interested in extending to all people in all communities the best possible medical care. The Constitution of the United States, the Bill of Rights and the "American Way of Life" are diametrically opposed to regimentation or any form of totalitarianism. According to available evidence in surveys, most of the American people are not interested in testing in the United States experiments in medical care which have already failed in regimented countries.

The physicians of the United States, through the American Medical Association, have stressed repeatedly the necessity for extending to all corners of this great country the availability of aids for diagnosis and treatment, so that dependency will be minimized and independence will be stimulated. American private enterprise has won and is winning the greatest war in the world's history. Private enterprise and initiative manifested through research may conquer cancer, arthritis and other as yet unconquered scourges of humankind. Science, as history well demonstrates, prospers best when free and unshackled.

Program

The physicians represented by the American Medical Association propose the following constructive program for the extension of improved health and medical care to all the people:

1. Sustained production leading to better living conditions with improved housing, nutrition and sanitation which are fundamental to good health; we support progressive action toward achieving these objectives.

2. An extended program of disease prevention with the development or extension of organizations for public health service so that every part of our country will have such service, as rapidly as adequate personnel can be trained.

3. Increased hospitalization insurance on a voluntary basis.

4. The development in or extension to all localities of voluntary sickness insurance plans and provision for the extension of these plans to the needy under the principles already established by the American Medical Association.

5. The provision of hospitalization and medical care to the indigent by local authorities under voluntary hospital and sickness insurance plans.

6. A survey of each state by qualified individuals and agencies to establish the need for additional medical care.

7. Federal aid to states where definite need is demonstrated, to be administered by the proper local agencies of the states involved with the help and advice of the medical profession.

8. Extension of information on these plans to all the people with recognition that such voluntary programs need not involve increased taxation.

9. A continuous survey of all voluntary plans for hospitalization and illness to determine their adequacy in meeting needs and maintaining continuous improvement in quality of medical service.

10. Discharge of physicians from the armed services as rapidly as is consistent with the war effort in order to facilitate redistribution and relocation of physicians in areas needing physicians.

11. Increased availability of medical education to young men and women to provide a greater number of physicians for rural areas.

12. Postponement of consideration of revolutionary changes while 60,000 medical men are in the service voluntarily and while 12,000,000 men and women are in uniform to preserve the American democratic system of government.

13. Adoption of federal legislation to provide for adjustments in draft regulation which will permit students to prepare for and continue the study of medicine.

14. Study of postwar medical personnel requirements with special reference to the needs of the veterans' hospitals, the regular army, navy and United States Public Health Service.

be in constant touch with our offices while fishing, juicy steaks synthesized entirely from yeast and broiled over synthetic hickory coals, sun-warmed and air-conditioned plastic houses with electric blankets on every bed, and automobiles, swift as the wind, silent as a tropical night, low hung and streamlined to raindrop perfection, with scratch-proof finish and puncture-proof tires. (The last specification is particularly desirable since the wheels will be practically unapproachable.) These things are being virtually promised to us by the wizards of industry as our reward for toppling the statue of fascism from its pedestal and preparing the latter for the advent of a shapely goddess, holding in one hand a miniature Diesel engine and in the other a pair of run-proof nylon stockings.

We are issued a timely warning, however, by Arthur W. Stevens, president of the Automobile Safety Association, in a letter published by the *Boston Herald* on May 24. The contents of this letter should be of special interest to the physicians of the Nation, concerned as they are more in public health than in the not inconsiderable fees to be derived from the patching up of injuries resulting from automobile accidents. The majority of these accidents, according to Mr. Stevens's plausible premise, are invited by the design of the present passenger car, which places the driver halfway back toward the rear of the car, "shutting off his effective view of the road and its hazards with an exaggerated hood, wide-flung fenders and thick corner posts." If we continue with the same trends in design, he adds, our highway massacre of the past will be resumed and will achieve even more appalling heights.

Mr. Stevens, in concluding his letter, quotes from an authority who had acquired a reputation for wisdom a thousand years before our Christian era began, — King Solomon, — who once declared, "Where there is no vision the people perish." We trust that the automobile designers of the postwar period will take note of Solomon's words and apply them in a practical manner to their own peculiarly important profession. We have had enough of violent death. If cars cannot be both graceful and safe, then the designers should at least try to approach the latter goal.

We should like to make still another suggestion while in the mood. It should not be too difficult to meter automobile horns to a certain small number of sound seconds per month; when the allotted time for hornblowing has run out, the car is put off the road until a new period begins. It's worth dreaming about.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BRESNIHAN — Frank N. Bresnihan, M.D., of Cambridge, died July 29. He was in his fifty-ninth year.

Dr. Bresnihan received his degree from Tufts College Medical School in 1913. He was a fellow of the American Medical Association.

His brother survives.

JACOBSON — Nathan L. Jacobson, M.D., of Lynn, died July 13. He was in his sixty-first year.

Dr. Jacobson received his degree from Maryland Medical College, Baltimore, in 1910. He was on the staffs of the Lynn and Union hospitals. He was a member of the Lynn Medical Association and the North Shore Medical Fraternity.

His widow, a son and a stepson survive.

RICHARDSON — Carl E. Richardson, M.D., of Franklin, died July 30. He was in his sixty-second year.

Dr. Richardson received his degree from Tufts College Medical School in 1907. He had been medical examiner of Norfolk County for twenty-one years. He was a fellow of the American Medical Association.

His widow, a son and a sister survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

POSTPONEMENT OF ELECTIVE TONSILLECTOMY

Inquiries are now being received by the Department of Public Health concerning the advisability of doing elective tonsillectomies during the summer months.

The present incidence of poliomyelitis is somewhat higher than that for the corresponding period of last year. Although this does not constitute the threat of a serious outbreak, the department is of the opinion that elective tonsillectomies should be postponed until the poliomyelitis season is over.

MISCELLANY

CHANGES IN ISOLATION AND QUARANTINE PROCEDURES FOR SCARLET FEVER

In line with modern thought on this common disease of childhood, the Board of Health [City of New York] radically revised its isolation and quarantine procedures in scarlet fever on December 12, 1944. The regulations now include

scarlet fever in the larger classification of "streptococcal sore throat, including scarlet fever," and change the isolation period in cases with no septic complications to the duration of the acute stage, the minimum period being seven days. The Board of Health further eliminated quarantine of household contacts to scarlet fever, making it no longer a requirement that such contacts stay out of school or work.

The action of the Board of Health was based on several factors. The first and most important of these is the fact that scarlet fever should not be considered a disease entity in itself, independent of other streptococcal throat infections. A large body of scientific work — clinical, bacteriological, immunological and epidemiological — indicates that the same hemolytic streptococcus (group A streptococci) which causes in one person septic sore throat, in another erysipelas and in a third puerperal sepsis may cause in a fourth the syndrome which for centuries has been known as scarlet fever. The type of clinical disease produced by infection depends on a number of factors — such as the previous history of streptococcal infection, the portal of entry of the infection and, to a certain extent, the characteristics of the particular strain of organism.

In many cases, the only distinction between septic sore throat and scarlet fever is the appearance of the rash, and there is ample evidence to indicate that the absence or presence of the rash is a phenomenon dependent on the individual's ability to withstand the so-called erythrogenic toxin of the hemolytic streptococcus. In other words, given two susceptible individuals exposed to the same hemolytic streptococcus, one person, because he is immune to the rash-producing mechanism, will have a sore throat without a rash, while the other person, nonimmune to this rash-producing toxin, will have scarlet fever. To have different regulations for persons suffering from the same disease, either with or without a rash, has for a considerable length of time been considered inconsistent.

The ineffectiveness of former quarantine measures was a second reason for the Board's decision. The age-old isolation measures, drastic as they were, had little or no effect on the incidence of streptococcal disease in general throughout the city. Moreover, from 1900 to the present there were different periods of isolation; yet, . . . there does not seem to be any close correlation between strict or liberal control of cases and the incidence of the disease. It seemed wiser, therefore, to put all streptococcal throat infections into one category with the same restrictive measures applying to all of them.

The majority of streptococcal throat infections, including scarlet fever, run their course in a week, and the hemolytic streptococcus responsible for the disease disappears in many cases or is reduced in numbers very considerably as soon as clinical recovery occurs. Since there are probably many more carriers of the hemolytic streptococci responsible for streptococcal throat infections including scarlet fever in the general population than in recovered cases, it was an undue hardship to require the strict isolation of convalescent streptococcal sore throat patients and scarlet fever convalescents until they were bacteriologically noninfectious, while allowing other carriers complete freedom of action.

The statement is occasionally made that complications of scarlet fever often do not set in until the second week, and that, consequently, cases should be isolated for at least two weeks. It is to be noted, therefore, that according to the Sanitary Code, cases of scarlet fever are isolated until recovery, but for a period of not less than one week. Complications following sore throat without a rash also frequently occur in the second week. Formerly such cases were not isolated.

A third reason for modifying the restrictions on scarlet fever was the experience which New York City shared with most of the United States and, in fact, with a great part of the world. Scarlet fever has become increasingly benign. It apparently reached a peak of severity during the last half of the nineteenth century and, since about 1875, has steadily become less severe. Available morbidity and mortality rates show a decrease in the case fatality rate of approximately 95 per cent from the earliest recorded rates to those of the present. This decline, however, has not been uniform, the northern states and urban areas showing more marked decreases than the southern states and rural areas. There seems to be no obvious explanation of this trend, but in the United States at the present time, there is no doubt that we are in a very mild phase of the cycle of the disease . . . deaths from scarlet fever in New York City are becoming very infrequent and the disease itself from the clinical standpoint certainly is a much milder one than is ordinarily associated with the word scarlet fever.

It was only after very careful consideration of the entire situation that the Board of Health, in line with the scientific evidence adduced above, modified the New York City regulations regarding scarlet fever. The New York State Department of Health, through its Public Health Council, adopted similar regulations. — Reprinted from *Quarterly Bulletin, Department of Health, City of New York, July, 1945.*

* * *

The above article explains, in more or less detail, the reasons for changes recently made by the New York City Department of Health regarding the isolation of patients with scarlet fever. These regulations were commented on editorially in the May 10 issue of the *Journal.* — ED.

CORRESPONDENCE

THE SUFFIX "–OSIS"

To the Editor: Having been educated at the feet of those Harvard scholars who challenge the world with their pronunciation of such words as "vertebral," "trachea" and "appendicitis," I have also developed somewhere along the line an acquired (or — shades of my Salem ancestors — could it be an atopic?) sensitivity to words ending in "–osis." Consequently I read with particular interest both the title and the substance of the article "Death from Sulfadiazine with Agranulocytosis, Jaundice and Hepatosis" by Ziegler et al. in the July 19 issue of the *Journal.*

Perhaps my Gould's dictionary is obsolete, but it does not give a definition of hepatosis. It does list "nephrosis (any renal disease)" and "polyposis (the condition of being afflicted with polyps)." What I should like to know is, Is a person with hepatosis afflicted with livers or does he just have any old hepatic disease?

GEOFFREY EDSALL, M.D.

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* * *

The *Journal* has often been criticized for its use of "-ic" and "-ical," but this is the first time that "-osis" has been so honored. According to Dorland's *American Illustrated Medical Dictionary* (twentieth edition), nephrosis means "any functional disorder of the liver." Since autopsy in the case referred to by Dr. Edsall failed to show a definite pathologic lesion, the word in question appears to be the proper one to have used. — ED.

SHATTUCK AND BOWDITCH

To the Editor: The leading article in the March 1, 1945 issue of the *Journal*, "Seventy-Five Years of Public Health in Massachusetts," is a timely reminder of one of those momentous conjunctions of individualities which, from time to time, have lighted new beacons and reset the course of progress.

Somewhat earlier, the names of Edwin Chadwick and Dr. John Simon had become associated in the English language of public health. About the same time, the names of Pasteur and Lister were coming to stand for new ideas in the science and the practice of surgery and medicine.

We all may be grateful to Merrill Champion for his terse restatement of long-recorded facts which made the Shattuck-Bowditch phenomenon of our own commonwealth one of those luminous combinations of personalities and ideas that is still a herald of light to illumine the present status of Massachusetts medicine and to project at least one ray beyond our present day.

Dr. Champion's account of Lemuel Shattuck as "pioneer" and Dr. Henry I. Bowditch as "organizer" is a well balanced sketch of outstanding events of the period 1849 to 1879, which have proved so full of meaning for public health in the Commonwealth and beyond our boundaries. Naturally, the pages of such an article cannot reproduce the complete

story. We may hope that Dr. Champion's paper will prompt many readers to look for themselves to those earlier records reposing for years in the recesses of our libraries, too easily overlooked by "modern" medicine and "modern" public health. The fuller meanings of the closely linked sympathy of these two outstanding characters of our past century unfold gradually to the thoughtful reader after the manner of the theme of Osler's "The Growth of Truth."

One part of the Shattuck–Bowditch story, evidently important in the time when our first state health authority was taking form, stems from Shattuck's enthusiastic conviction that necessary agents of the "sanitary reform" he envisioned and advocated so zealously must be physicians of such knowledge and character, as were still rare attributes of the profession of his time. As part of the argument of his report to the legislature in 1850 for more adequate public measures in the prevention of disease, witness this statement concerning duties of medical officers of health in Appendix XI of the 1850 Commission Report: "Preventive medicine, while it constitutes a special [science], is in itself the highest and most useful branch of medicine and requires in its missionaries a correspondingly long and special study to become useful promulgators of its doctrines and workers in its cause." On one of the very early pages of this same report, witness also his reference to the famous question, "Who is the physician who is an honor to his profession?" And the immortal answer, in words attributed to Hippocrates himself: "He who has merited the esteem and confidence of the public by profound knowledge, long experience and consummate integrity; who has been led through all the circle of the sciences. . . ."

The complement to Mr. Shattuck's high ideals of the unrealized social potentials of the medical profession is Dr. Bowditch's high esteem of Mr. Shattuck personally, of the public ideals that Shattuck represented and of his part in the getting the idea of preventive medicine officially recognized and accepted in the Commonwealth. Glimpses of this part of the picture appear in several accessible records. *The History of the Massachusetts Medical Society*, by Dr. W. L. Burrage, tells much and implies more. Dr. Bowditch himself, commemorating the first century of medicine in the United States in an address before the National Medical Congress in Philadelphia in 1876, referred to Shattuck as one of two outstanding characters of the English-speaking world "prominent in their relation to the third epoch or that in which the medical profession is aided by the laity." In speaking further of Shattuck, he said: "There is no doubt that he, as a layman, quietly working, did more toward bringing Massachusetts to correct views on this subject than all other agencies whatsoever."

Pioneers of Public Health, by M. E. M. Walker, contains a chapter on Shattuck along with those on Jenner, Pasteur, Lister and other such notables. This same manual refers also to that portion of Dr. Bowditch's centennial address of 1876 which reads as follows:

> Twenty-five years ago, viz. in 1850, a report of the Sanitary Commission of Massachusetts was printed by order of the Legislature. It was written chiefly, if not entirely, by a layman — Lemuel Shattuck, Esquire, an earnest sanitarian of that day. . . . As I read it now after a lapse of a quarter of a century since it was written and presented to the Legislature, I wonder at the wisdom of its suggestions and learn much from them. . . . I remember Mr. Shattuck well — calm in his perfect confidence in the future of preventive medicine to check disease; he walked almost alone the streets of his native [adopted] city — not only unsustained by the profession but considered by most of them an offense of his candid advocacy of what seemed to the majority of physicians to be out of the layman's sphere and withal of trifling moment compared with our usual routine of so-called practice.

Thus, in 1876, Dr. Bowditch, one-time secretary of the Massachusetts Medical Society and one-time secretary of the American Medical Association, chosen to review for assembled physicians of all nations the first century of medicine in the United States, declared concerning the "third epoch" or that in which the medical profession had been aided by the laity, "The ruling idea of this epoch is still in its infancy but shows by what it has already accomplished, trivial though this performance may seem at first glance to be, its inherent and great power; its objects are vastly wider than those of any preceding epoch." In that courageous declaration of young American medicine there appeared a vigorous new witness to the ancient truth that from time to time in the affairs of men, traditional antitheses unite in a new birth of freedom in procreative thought and action.

In the first annual report (1870) of the State Board of Health "to the honorable Senate and House of Representatives," Dr. Bowditch, as secretary, defined "the essential principles of action" of the new board and the place of physicians in carrying out those principles of action in these words:

> By the careful and comprehensive study of these various laws [of health and life] and their relations, the highest department of the physician's art is brought into operation; but no man or private body of men has the ability to study and develop this department as a free commonwealth can do when acting through the agency of a few persons who are devoted to this object and who come willingly to the work and armed with the power and ample means of the state.

In terms of individual life, seventy-five years means venerable maturity. In terms of growth of a social discipline, it usually means something quite different. The "ruling idea" of that epoch in which the medical profession was aided by the laity was only in its infancy when it imparted its drive to the developments that have become "seventy-five years of public health in Massachusetts" and that have lent their sanction to and determined the pattern of most of our subsequent public-health legislation.

What can this seventy-fifth anniversary report tell of the present "physical stature" and "mental age" of that promising infant idea, which Dr. Bowditch spoke of as the "ruling idea" of the new epoch? Today that same idea has rich possibilities that Shattuck and Bowditch could hardly have imagined. Compared with their time, this is a time of vastly amplified power and means, "professional" and "lay," within the society that is our commonwealth operating under the liberal principles of our social philosophy and of our chosen form of government. The stirring environment of this larger world, which sets new premiums on physical power and moral and spiritual stamina, also begins to define new objectives to give direction to this amplified power and means. Furthermore, against the background of the Shattuck–Bowditch time, we are a profession generously qualified to exercise our responsibilities in an enlarged "practice" in sincere, fearless, forward moving collaboration with the peoples who are today's "laity" through their agencies of government and other agencies of organized power and action.

The names of Pasteur and Lister have long stood for an epoch of the advance of medicine as a biologic science and art. Is it a too daring draft on our account with destiny to expect an equally distinguished maturity for the vigorous Shattuck–Bowditch conception of medicine as a social science and a growing social practice carrying the full benefits of medical knowledge to every family and every person in the Commonwealth? Of that idea which he considered then "the ruling idea — still in its infancy," Dr. Bowditch said in 1876, "Its early manhood will not be reached until far toward the termination of the next century."

Again, we thank Merrill Champion for his timely contribution to the "child hygiene" of Massachusetts medicine.

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MIDDLESEX MEDICAL SOCIETY

To the Editor: In "The History of Middlesex North District Medical Society," which appeared in the July 12 issue of the *Journal*, Dr. Gardner states that the first medical association in Middlesex County was formed in 1829. Thacher's *American Medical Biography*, in its account of the Honorable Oliver Prescott, "M.D., M.M.S.S. and A.A.S.," states on page 429 of Volume I that he was "president of the Middlesex Medical Society during the whole period of its existence." Dr. Prescott was born in Groton in 1731 and died (of a pectoral dropsy) in 1804. What his "Middlesex Medical Society" amounted to

and how long it lasted I do not know, but it probably was organized in the eighteenth century.

This letter intends to supplement rather than challenge Dr. Gardner's excellent paper, and it perhaps may call forth other fragments concerning early medical days in Middlesex County.

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MEDICAL SCHOOLS AND COMPULSORY MEDICAL INSURANCE

To the Editor: This is a note on a possible solution of the question as to the position of medical schools under compulsory medical insurance.

This year the Governor of California introduced a compulsory health insurance bill (A.B. 800). The Congress of Industrial Organizations, which had long been studying health insurance, introduced another bill (A.B.449) that differed from the Governor's on several important details.

The Governor's bill made no reference to medical schools. After the Governor, however, had consulted with the deans of the four schools in the State he announced that if the schools should happen to treat beneficiaries under the act they would not ask that more than their expenses be covered and that so far as teaching was concerned "medical indigents" would still be available.

Under the C.I.O. bill, indigents received benefits and the number of those covered by the provisions of service was so large that the point was raised that most of the people who are now coming to the medical schools might go to private doctors. The authors of the C.I.O. bill recognized the seriousness of this possibility in regard to medical teaching. They looked on medical schools as the organizations best equipped to forward that maintenance and improvement of the quality of medical care without which a mere extension in quantity might prove a dubious blessing. Therefore, the bill provided that representatives of medical schools be appointed on both the central and local governing bodies under the act. To make sure that these representatives should be in close touch with advancing knowledge it was required that they should be selected from those who were in whole-time investigation and teaching. To avoid the danger of bureaucratic or political interference it was provided that medical schools, or any other group capable of giving complete and adequate medical service, might be paid a lump sum for all they did, leaving them free to spend the money in any way they desired. Universities might thus give some of it to research work and some of it to younger men who now work for nothing. The indications were that the amount of money that would be thus put at the disposal of the universities might be so large that the present crippling of medical-school work from lack of money would largely disappear. With practice passing more and more into the hands of a series of interconnected groups of doctors, working in rural areas around medical centers, in district towns around hospitals and coming to an apex in medical schools, it was felt that people would be eager to be treated by medical-school groups and that the great majority would welcome a discussion of their medical problems with medical students.

The reaction of medical students to these proposals in the C.I.O. bill was interesting. At the University of California Medical School, 106 students signed a petition to their dean in which the advantages of the plan for all medical schools were stressed. At Stanford, 209 students, practically the entire student body who could be reached in the time available, sent a petition to the Dean, the President, the Board of Trustees and the Alumni Association urging them to work for the adoption of the medical-school provisions of the bill. This substantial unanimity was achieved because the question of the advisability of compulsory medical insurance was not raised. The point that they were making was that if compulsory insurance became law they wanted their medical schools to take an active part in maintaining and advancing the quality of the care given to the people, to accept from the government the money due to the schools for the services they rendered and to maintain their freedom by keeping the disposal of the money received in the hands of the universities.

Although this bill was killed in committee, the question of the status of medical schools under compulsory medical insurance will be raised again, and so the plan that was proposed is still important as the first constructive solution of a difficult problem that has found expression in concrete legislative form.

T. ADDIS

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BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Woman Asks the Doctor. By Emil Novak, M.D., associate in gynecology, Johns Hopkins University School of Medicine, and gynecologist, Bon Secours and St. Agnes hospitals. 8°, cloth, 130 pp., with 11 illustrations. Second edition. Baltimore: Williams and Wilkins Company, 1944. $1.50.

Much new material has been added to this second edition of a popular work on menstruation and its disorders. The author, who is an eminent gynecologist, discusses only those problems in which all women are interested and those in which he believes they most need instruction. This manual is recommended for collections on popular medicine.

NOTICES

ANNOUNCEMENT

Dr. Bennett Solomon announces the reopening of his office at 145 State Street, Springfield 3.

AMERICAN BOARD OF OPHTHALMOLOGY

The American Board of Ophthalmology announces the following examinations in 1946: Chicago, January 18 to 22 inclusive; Los Angeles, January 28 to February 1 inclusive; New York City, May or June; and Chicago, October. Owing to transportation difficulties the examination, originally scheduled for October, 1945, in Chicago, has been postponed.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, AUGUST 23

FRIDAY, AUGUST 24

*9:00–10:00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.

10:50 a.m. Bacterial Infections of the Skin. Dr. George Morris. (Postgraduate clinic in dermatology and syphilology.) Amphitheater, Mallory Building. Boston City Hospital.

MONDAY, AUGUST 27

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, AUGUST 28

*9:00–10:00 a.m. Medical clinic. Infants' Hospital.

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, AUGUST 29

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

SEPTEMBER 13. The Hemorrhagic Diseases. Dr. William Dameshek. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

SEPTEMBER 17. American Public Health Association. Page 572, issue of November 30.

OCTOBER 1–6. Medicolegal conference and seminar. Page 776, issue of June 28.